NEUROCOGNITIVE DEFICITS IN PEDIATRIC OBESITY

A Dissertation
submitted to the Faculty of the
Graduate School of Arts and Sciences
of Georgetown University
in partial fulfillment of the requirements for the
degree of
Doctor of Philosophy
in Psychology

By

Alaina L Pearce, M.A.

Washington, DC
November 17, 2017
ABSTRACT

In the United States, 20% of adolescents suffer from obesity (body mass index—BMI—above the 95th percentile) and 8% of adolescents suffer from severe obesity (BMI 120% above the 95th percentile). Obesity carries increased risk for medical conditions with high morbidity (e.g., cardiovascular disease, diabetes), poor sleep health, and psychopathology. In children, these risks are accompanied by lower academic achievement and worse social (e.g., discrimination) and psychological (e.g., self-esteem) outcomes. When examining cognition functioning, deficits in executive function (i.e., working memory, inhibitory control, and cognitive flexibility), motivation (i.e., reward sensitivity and reward-related decision making), and memory have been shown to be particularly relevant for the regulation of obesogenic behaviors (i.e., behaviors that contribute to risk for obesity). Simultaneously, comorbidities of obesity, such as chronic inflammation, may have deleterious effects on the neural functioning subserving these cognitive processes. The three studies included in this dissertation were conducted with the goals of 1) determining the scope and specificity of cognitive deficits in pediatric obesity; 2) identifying potential confounding (intelligence, socio-demographic characteristics) and mediating (medical and psychopathological) factors related to cognitive deficits in pediatric obesity; and 3) examining the neurological underpinnings of observed cognitive deficits in pediatric obesity.
This thesis is dedicated to all of my mentors, colleges, friends, and family who have supported this journey. To my husband, David, I am so grateful for your love and support and for upholding your promise to never let me run out coffee! Stella, I want to thank you for keeping me on my toes with your love and sassiness.

Sincerely,

Alaina L. Pearce
# TABLE OF CONTENTS

CHAPTER I: GENERAL INTRODUCTION ................................................................. 1

MODEL OF PEDIATRIC OBESITY ........................................................................... 3

FEED-FORWARD MODEL OF PEDIATRIC OBESITY: OBESOGENIC BEHAVIORS .................................................................................................................. 4

FEED-BACKWARD MODEL OF PEDIATRIC OBESITY: NEURO-INFLAMMATION ........................................................................................................... 6

INTEGRATED MODEL OF PEDIATRIC OBESITY ................................................. 8

OUTLINE OF DISSERTATION STUDIES ............................................................... 9

CHAPTER II: EXECUTIVE AND REWARD-RELATED FUNCTION IN PEDIATRIC OBESITY: A META-ANALYSIS ................................................................. 11

METHODS ........................................................................................................... 15

LITERATURE SEARCH ....................................................................................... 15

CODING AND DATA EXTRACTION .................................................................. 17

DATA ANALYSIS ................................................................................................ 23

STATISTICAL MODEL ....................................................................................... 24

HETEROGENEITY ............................................................................................... 24

PUBLICATION BIAS .......................................................................................... 25

RESULTS ............................................................................................................ 25

RANDOM INTERCEPT MODELS (TABLE II-3) ............................................... 26

IQ AND SES ...................................................................................................... 26

OVERALL AND COMPONENT PROCESS MODELS ....................................... 27
SLEEP HEALTH.............................................................................................................46
PSYCHOPATHOLOGY ....................................................................................................46
MEDIATION ANALYSES ..............................................................................................46
DISCUSSION ..................................................................................................................48

CHAPTER IV: ALTERED NEURAL BASES OF MEMORY, EXECUTIVE
FUNCTION, AND REWARD IN ADOLESCENT OBESITY ..............................................53
MATERIALS AND METHODS ..................................................................................56
PARTICIPANTS .............................................................................................................56
EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS ....................................57
WORKING MEMORY ...............................................................................................58
REWARD ANTICIPATION .........................................................................................58
REWARD-RELATED DECISION-MAKING ..............................................................59
EPISODIC MEMORY ..................................................................................................59
IMAGE ACQUISITION PARAMETERS ......................................................................60
STATISTICAL ANALYSES .........................................................................................61
RESULTS ......................................................................................................................62
WORKING MEMORY ...............................................................................................62
REWARD ANTICIPATION .........................................................................................65
REWARD-RELATED DECISION-MAKING ..............................................................67
EPISODIC MEMORY ..................................................................................................69
DISCUSSION ................................................................................................................71

CHAPTER V: GENERAL DISCUSSION ......................................................................77
IMPLICATIONS: NEUROCOGNITIVE FUNCTIONING ..............................................78
LIST OF FIGURES

Figure I-1. Distributions of BMI for US Adults from 1971-2014. ...........................................1
Figure I-2. BMI Estimates for US Children and Adolescents in the 50th and 95th Percentiles from 1988-1994 and 2011-2014.................................................................2
Figure I-3. Integrated Model of Pediatric Obesity. .................................................................4
Figure II-1. Flowchart Depicting Results and Methods of the Systematic Review............16
Figure II-2. These Plots Depict Significant Moderators of the Effect of Obesity on Executive Abilities.................................................................32
Figure III-1. Separate Multiple Mediation Models are Depicted for the Behavioral Regulation and Metacognitive Indices of the Behavioral Rating Inventory of Executive Function .................................................................47
Figure IV-1. Clusters Showing Greater Activation for Adolescents With than Without Obesity During the N-back Task Indexing Executive Function, Controlling for Mean Motion Scan-to-Scan and Age .................................................................64
Figure IV-2. Anticipation of Reward for the Showing Monetary Incentive Delay Task, Controlling for Mean Motion Scan-to-Scan and Age .................................................................66
Figure IV-3. Clusters Showing Greater Activation for Adolescents Without than With Obesity During Encoding for Episodic Memory, Controlling for Mean Motion Scan-to-Scan and Age .................................................................70
LIST OF TABLES

Table II-1. Study Characteristics .................................................................19
Table II-2. Model Characteristics .................................................................26
Table II-3. Model Results .............................................................................26
Table II-4. Sensitivity Results .....................................................................30
Table III-1. Demographic Characteristics ..................................................42
Table III-2. Task Performance .....................................................................45
Table IV-1. Demographic Characteristics ....................................................57
Table IV-2. Performance During Episodic Memory, N-Back, Monetary Incentive Delay, and Balloon Analog Risk Taking Tasks .................................................................63
Table IV-3. Peak Activations from Clusters Showing Greater Activation for Adolescents With than Without Obesity During the N-back Task Indexing Executive Function, Controlling for Mean Motion Scan-to-Scan and Age .................................................................65
Table IV-4. Group x Reward Value Analysis of Variance: Peak Activations from Significant Clusters for the Monetary Incentive Delay Task, Controlling for Mean Motion Scan-to-Scan and Age .................................................................69
Table IV-5. Peak Activations from Clusters Showing Greater Activation for Adolescents Without than With Obesity During Encoding for Episodic Memory, Controlling for Mean Motion Scan-to-Scan and Age .................................................................69
CHAPTER 1: GENERAL INTRODUCTION

The global obesity epidemic began with steep increases in the prevalence of obesity during the 1970’s for adults (Pak, Ferreira, & Colson, 2016) and during the 1980’s for children (Strauss & Pollack, 2001). In the United States, the mode of the distribution of adult body mass index (BMI; kilograms divided by meters squared) has shifted upward and the positive tail has thickened such that 37.7% of adults meet criteria for obesity (BMI > 30) and 7.7% of adults meet criteria for class 3 obesity (BMI > 40; Figure I-1; Flegal, Kruszon-Moran, Carroll, Fryar, & Ogden, 2016; Pak, Ferreira, & Colson, 2016).

Figure I-1. Distributions of BMI for US Adults from 1971-2014.

PDF: probability density function.
Adapted from Pak et al. (2016).

The epidemic rise of pediatric obesity followed a similar pattern with an overall increase of the prevalence of obesity (BMI > 95th percentile for age and gender) in addition to a disproportionate increase of the prevalence of severe obesity (BMI 120% above the 95th percentile cutoff; Figure I-2). In the United States, 20.5% of adolescents (12-19 years) and 17.5% of children (6-11 years) meet criteria for obesity and 7.8% of adolescents and 5.6% of children meet criteria for severe obesity (Ogden et al., 2016). Despite increased research focus (~7,475 publications to added to PubMed) pertaining to pediatric obesity,
existing models of the causes and consequences are just beginning to integrate hypothalomic pathways with hedoic and neurocognitive components. The goal of this dissertation is to help elucidate the impact of neurocognitive deficits in pediatric obesity.

Pediatric obesity is associated with a series of deleterious consequences spanning medical, psychosocial, cognitive, and academic outcomes (Halfon, Larson, & Slusser, 2013; Kamijo et al., 2012; Pulgarón, 2013; Reinert, Po'e, & Barkin, 2013), resulting in a quality of life equivalent to that of pediatric cancer for adolescents with severe obesity (Schwimmer, Burwinkle, & Varni, 2003). Children and adolescents with obesity have elevated risk for medical comorbidities with high mortality such as cardiovascular disease, diabetes, obstructive sleep apnea, and nonalcoholic fatty liver disease, with the likelihood of experiencing multiple comorbidities increasing with increasing BMI (Freedman, Mei, Srinivasan, Berenson, & Dietz, 2007). A child with obesity is estimated to incur an additional $19,000 of lifetime direct medical cost compared to a peer with healthy weight (Finkelstein, Graham, & Malhotra, 2014), which results in a cumulative increase costs of $17-$25 billion in direct medical costs for the approximately 4 million 5th graders in the United States (Levitt, Jackson, & Morrow, 2016). In addition to direct

costs, psychopathological, psychosocial, and cognitive co-morbidities result in increased indirect costs (i.e., loss of productivity). Currently, there is no estimate for the lifetime indirect cost of pediatric obesity in the United States, however, a study in Germany showed 3-4.5 times higher indirect costs associated with having met criteria for overweight or obesity during at least some part of childhood (Sonntag, Ali, & De Bock, 2016). With 55% of children and 80% of adolescents with obesity continuing to meet criteria for obesity after the age of 30 (Simmonds, Llewellyn, Owen, & Woolacott, 2016), it is clear that understanding the causes and consequences of obesity is not only important for pediatric health and development, but also for the future health and productivity of the United States.

**Model of Pediatric Obesity**

The etiology of pediatric obesity is simultaneously straight-forward and incredibly complex. Ultimately, obesity results from an energy imbalance due to the consumption of more caloric energy than is expended, with a consistent daily energy imbalance of only 2% capable of leading to the development of obesity in children (Goran, 2001). However, the etiology becomes less clear when one asks the question of why some children fail to regulate their energy balance and obesogenic behaviors (e.g., emotional eating, consuming energy dense foods, sedentary behavior) while others do so successfully. Multiple risk factors for obesogenic behaviors have been identified including characteristics of neighborhoods (e.g., food deserts and safety), schools (e.g., physical education and school lunch quality), families (e.g., parental obesity, education and socio-economic status), and the individual (e.g., psychosocial and cognitive functioning and psychopathology; Campbell, 2016). Although the development of
Pediatric obesity is influenced by environmental and social factors, understanding how individual characteristics relate to risk for obesity is critical for prevention and intervention. This dissertation proposes a model of pediatric obesity that integrates feed-forward individual risk factors for obesogenic behaviors and feedback consequences that result from the development of obesity (e.g., medical comorbidities; Figure I-3).

**Figure I-3. Integrated Model of Pediatric Obesity.** Activation images reflect the likelihood of activation across studies given the use of the terms reward (red), executive function/executive control (blue), and episodic memory (green). Activation images were generated by using Neurosynth.org’s automated and custom meta-analyses.

**Feed-Forward Model of Pediatric Obesity: Obesogenic Behaviors**

When considering individual risk factors for obesogenic behaviors, studies have begun to emphasize the role of three cognitive processes: 1) executive function; 2)
reward sensitivity; and 3) memory. Executive function, which is a set of cognitive
processes employed during goal directed behavior (i.e., inhibition and working memory; Diamond, 2013), has been negatively associated with obesogenic behaviors such that children with better executive abilities were more likely to maintain a healthy body weight into adolescence (Duckworth, Tsukayama, & Geier, 2010), while children with worse executive abilities had greater risk for maladaptive eating behaviors (e.g., emotional overeating; Groppe & Elsner, 2015) and snack food intake (Riggs, Chou, Spruijt-Metz, & Pentz, 2010). Similarly, greater reward sensitivity in children was predictive of greater intake of fast food and sugar sweetened beverages (De Decker et al., 2016). Reduced ability to delay gratification in young children (ages 2-5 years) was also predictive of an accelerated rate of weight gain through childhood (Francis & Susman, 2009) and obesity status during pre-adolescence (age 10; Graziano, Kelleher, Calkins, Keane, & Brien, 2013). Lastly, although not yet examined in children and adolescents, worse episodic memory in adults was predictive of more unconstrained and emotional eating while better episodic memory was associated with avoidance of fatty foods (Martin, Davidson, & McCrory, 2017). Thus, executive, reward, and mnemonic processes may play causal roles in the development of pediatric obesity through their influence on obesogenic behaviors (Berthoud, Munzberg, & Morrison, 2017; Dohle, Diel, & Hofmann, 2017; Hargrave, Jones, & Davidson, 2016).

Although executive, reward, and mnemonic processes have independent associations with obesogenic behaviors and obesity, it is important to consider how they interact to regulate obesogenic behaviors. In a study of European children and adolescents, the association between unhealthy snacking behavior and sensitivity to food
environments was modulated by self-regulation abilities (Stok et al., 2015), indicating executive functioning may play an important role in inhibiting reward-related motivation (Dohle et al., 2017). Additionally, working memory, which is the ability to hold and manipulate information in the mind (Diamond, 2013), may enable self-regulation by maintaining long-term goals in mind (e.g., making healthier food choices) in order to resist temptations (Dohle et al., 2017). Similarly, food and meal related memories may influence reward-related decision making through the inhibition of appetitive cues or memory of food rewards with deficits in episodic memory resulting in more automatic or habitual responses to food rewards (Higgs, 2016). Indeed, although self-reported hunger at the end of a meal is directly related to food consumption, reports of hunger 2-3 hours post meal were more strongly related to the memory of amount eaten than true caloric intake (Brunstrom et al., 2012). Taken together, executive functioning and episodic memory appear to modulate stimulus-driven reward response and motivation in order to inform adaptive reward-related decision making.

**Feed-Backward Model of Pediatric Obesity: Neuro-Inflammation**

Neurocognitive deficits are important risk factors for pediatric obesity, however, deleterious comorbidities associated with obesity may further exacerbate these deficits. Obesity causes chronic, low-grade systemic inflammation due to the enlargement of adipocytes (i.e., fat cells; Spyridaki, Avgoustinaki, & Margioris, 2016), which trigger native macrophages (i.e., white blood cells) to release pro-inflammatory cytokines (Capuron & Miller, 2011). Local inflammation of adipose tissue spreads systemically when macrophages accumulate in adipose tissue and become pro-inflammatory (Spyridaki et al., 2016). Prior to the development of other medical co-morbidities (e.g.,
insulin resistance), this chronic “metabolic” inflammation (Margioris, 2009) contributes to neuro-inflammation (A. A. Miller & Spencer, 2014; Spyridaki et al., 2016) through cytokines. Circulating inflammatory cytokines are able to bypass the blood-brain barrier (BBB) in two ways: 1) directly through the BBB due to increased permeability associated inflammation and high fat diets; and 2) through hypothalamic circumventricular organs (e.g., arcuate nucleus) and cytokine receptors (A. A. Miller & Spencer, 2014). Neuro-inflammation has been shown to cause local insulin and leptin resistance in the hypothalamus, which regulates appetite though homeostatic signaling for leptin and insulin (Thaler & Schwartz, 2010). Although there has been less research on non-hypothalamic regions, neuro-inflammation due to cytokines or activated neuronal immune response (microglia and astrocytes) is thought to lead to neurodegeneration, decreased neurogenesis, and increased oxidative stress, which together may cause changes in cellular signaling, neurocircuitry, and atrophy. Together, this cascade of neuro-inflammatory processes and consequence may result in worse neurocognitive function (A. A. Miller & Spencer, 2014; Spyridaki et al., 2016).

There is growing evidence for a causal link between neurocognitive deficits and obesity related inflammation and metabolic dysregulation. Systemic inflammation due to obesity has been shown to mediate the association between obesity and worse fluid intelligence in adults (Spyridaki et al., 2014). Additionally, adolescents with obesity have greater whole brain and hippocampal atrophy (Tirsı, Duong, Tsui, Lee, & Convit, 2013) and reduced cortical thickness (Yau, Kang, Javier, & Convit, 2014) relative to peers with healthy weight. Most convincing, though, is the evidence that shows cognitive and neural changes after weight loss. A recent review showed that bariatric surgery was consistently
associated with improved executive and memory function (Thiara et al., 2017), with improvement lasting up to 48 months after surgery (Alosco et al., 2014). Although the causal links between obesity related neuro-inflammation and neurocognitive function have yet to be fully elucidated, it is likely that initial neurocognitive deficits associated with pediatric obesity worsen after obesity develops.

**Integrated Model of Pediatric Obesity**

Together, findings suggest a model of pediatric obesity where cognitive deficits are both cause and consequence of obesity (Figure I-3). Poor executive, reward, and mnemonic functioning appear to predispose children to engage in fewer protective health-related behaviors while also increasing the likelihood of engaging in obesogenic behavior, potentially leading to a habitual energy imbalance and weight gain. Chronic, systemic inflammation develops along with obesity, potentially contributing to neuro-inflammation. It is hypothesized that neuro-inflammation influences the maintenance and promotion of obesity through two pathways: 1) hypothalamic inflammation leads to local leptin and insulin resistance, disrupting appetite suppressing signaling; and 2) non-hypothalamic inflammation may alter neuronal structure and function, resulting in worse neurocognitive function. Thus, the inflammatory consequences of obesity contribute to a feedback cycle that reinforces the maintenance of obesity though neuronal and behavioral pathways. As this cycle is maintained, development of other comorbidities such as insulin resistance, metabolic syndrome, and sleep apnea may compound the effects of neuro-inflammation on neurocognitive function.
Outline of Dissertation Studies

Although the integrated model of pediatric obesity outlined above is supported by a series of studies, it is better interpreted as a set of hypotheses than an established model of pediatric obesity. The current dissertation focused on the feed-forward components of the proposed model in order to examine the breadth and specificity of neurocognitive deficits in pediatric obesity. The role of important confounding factors (i.e., sleep, socio-economic status) were also examined to address how contextual and medical risk factors may impact the association between neurocognitive function and pediatric obesity. In order to accomplish these goals, a series of three studies were completed using different methodological approaches: 1) a meta-analytic review of the literature; 2) a behavioral study using task based and neuropsychological assessments; and 3) a functional magnetic resonance imaging (fMRI) study.

The first study is a quantitative review which aimed to 1) estimate the effect of pediatric obesity on executive function and reward-related decision making and 2) evaluate how the observed effects of obesity were moderated by sample (e.g., age, gender, intelligence, and socio-economic status) and study/task characteristics (e.g., categorical/continuous variable, food stimuli). The review was limited to studies that included children and adolescents without known medical comorbidities related to pediatric obesity in order to eliminate the potential confounding effects of medical or psychopathological comorbidities of obesity. This was the first quantitative review of neurocognitive deficits in pediatric obesity that not only estimated the overall effect of obesity, but also examined factors that may moderate the negative effect of obesity.
The second study is a behavioral study which aimed to 1) test executive and reward function in children and adolescents (7-18 years old) with either healthy weight or obesity with no known medical comorbidities and 2) examine sleep health and parent-reported psychopathology as potential mediators of observed deficits in pediatric obesity. This was the first study to test the independent mediating effects of sleep health and psychopathology on the association between cognitive deficits and pediatric obesity. Additionally, this was the first study to use a Bayesian decision making model to assess process biases during reward-related decision making in pediatric obesity.

The third study is a fMRI study which aimed to 1) examine the neural underpinnings of executive function, reward anticipation, and encoding of episodic memory in adolescents (14-19 years) with either severe obesity or with healthy weight and 2) replicate behavioral findings from the second study for executive function and reward-related decision making. This was the first study to examine neural activation (i.e., blood-oxygen-level dependent—BOLD—activity) during executive and reward tasks without the use of food stimuli in adolescents with obesity and the first to examine episodic encoding in adolescents with obesity.

Together these studies provide novel findings that better specify the nature of neurocognitive deficits associated with pediatric obesity and begin to identify potential targets for prevention and intervention.
CHAPTER II: EXECUTIVE AND REWARD-RELATED FUNCTION IN PEDIATRIC OBESITY: A META-ANALYSIS


The epidemic rise in overweight children was recognized over 15 years ago (Strauss & Pollack, 2001), however, the prevalence of obesity (body mass index—BMI—above the 95th percentile for age and gender) in adolescence (12-19 years) has continued to rise with over 20% currently obese (Ogden et al., 2016). Prevalence remains steady 17.5% in younger children (6-11 years). In addition to increased risk for medical and psychopathological comorbidities during childhood (Halfon et al., 2013) and later in adulthood (Martinson & Vasunilashorn, 2016; Reilly & Kelly, 2011), pediatric obesity is associated with worse social (Krukowski et al., 2009), cognitive (Reinert et al., 2013), and academic outcomes (Bisset, Fournier, Janosz, & Pagani, 2013; Krukowski et al., 2009). Models of obesity point to the centrality of cognitive factors such as executive and reward-related processes that may serve to promote and maintain obesity through their influence on obesogenic behavior such as consumption of fatty and sweet palatable foods and activity choices (Carnell, Gibson, Benson, Ochner, & Geliebter, 2011; Raman, Smith, & Hay, 2013). In light of the growing literature of studies examining these cognitive functions in pediatric obesity, we conducted a meta-analysis with the goal of drawing definitive conclusions about their status in children with obesity and moderating socio-demographic factors (e.g., socio-economic status—SES, age, gender).
Executive function subsumes voluntary regulatory processes that enable flexible goal-directed behavior, which in association with reward processing guides decision making (Steinbeis & Crone, 2016). The conceptual framework for the present investigation takes a cognitive neuroscience perspective, which posits that a set of general-purpose control processes enabled by the prefrontal cortex serve to regulate complex cognition (Diamond, 2013). Confirmatory factor analysis of simple and complex tasks considered to tap executive functions has identified three control processes: 1) attending to and holding contextually appropriate stimuli and responses in mind temporarily (indexed by tasks and measures of attention and working memory); 2) inhibiting inappropriate responses (indexed by tasks of inhibition and interference, sometimes termed cognitive control and questionnaires of impulsive traits), and 3) flexibly shifting responses as context changes (indexed by tasks and measures of cognitive flexibility or shifting (Miyake et al., 2000). These control processes interact with implicit and explicit reward processes which entail: 1) affect, which encompasses hedonic value or “liking” and “pleasure”; 2) learning of reward contingencies; and 3) motivation, defined as “wanting” driven by saliency and goal-directed action plans driven by desire (Berridge & Robinson, 2003). The present investigation focused on studies examining behavioral outcomes of reward-related decision making as measured by delay of gratification and delayed discounting tasks manipulating rewards. These tasks require the integration of control processes with “liking” and “wanting” reward-related processes and is known to be subserved by connections of the prefrontal cortex with striatal regions (Horstmann, 2017).

Together, the interaction of executive and reward processes determines a variety
of developmental outcomes. Better executive abilities are associated with better academic achievement (Samuels, Tournaki, Blackman, & Zilinski, 2016) and social-emotional development (Best & Miller, 2010). In the context of decision making about risk and reward, better executive function is associated with reduced risky behavior (e.g., drinking, smoking; Pharo, Sim, Graham, Gross, & Hayne, 2011), higher likelihood to change or modify risky behavior after facing negative consequences (Turanovic & Pratt, 2012), and lower delinquency and fewer financial difficulties later in adulthood (Moffitt et al., 2011). Thus, executive and reward functioning is a cornerstone of child and adolescent development with consequences extending into adulthood, highlighting the need to better understand their association with pediatric obesity.

Executive and reward function is associated with both the promotion and maintenance of obesity by influencing both healthy and obesogenic behaviors (Carnell et al., 2011; Raman et al., 2013). Better inhibitory control has been associated with increased likelihood of completing a planned physical activity or healthy food choice in adults (Hall, Fong, Epp, & Elias, 2008) and was associated with more fruit/vegetable intake and engagement in physical activity in children (Riggs et al., 2010). Children with better executive function at the end of elementary school were also more likely to maintain a lean body weight at the end of junior high (Duckworth et al., 2010). Conversely, poor executive abilities in children have been associated with greater snack food intake and sedentary behavior (Riggs et al., 2010) and increased risk for maladaptive food behavior (e.g., emotional overeating; Groppe & Elsner, 2015), while increased reward sensitivity in children has been associated with greater intake of fast food and sweetened beverages (De Decker et al., 2016). Additionally, worse delay of
gratification and self-regulation in early childhood (2 and 4 years) were associated with higher BMIs in later childhood (Seeyave et al., 2009), pre-adolescence (Graziano et al., 2013), and adulthood (Schlam, Wilson, Shoda, Mischel, & Ayduk, 2013), while worse executive function was associated with less successful weight loss (Nederkoorn, Jansen, Mulkens, & Jansen, 2007) in children. Prevention and intervention efforts would be served by knowing the magnitude of executive and reward-related decision making deficits in children and adolescents with obesity and whether these deficits are moderated by socio-demographic factors.

The effect of obesity on executive function appears to be moderated by a variety of demographic factors. Variability in general intelligence, as measured by IQ, and SES are independently associated with risk for pediatric obesity (Shrewsbury & Wardle, 2008) and executive dysfunction (Ardila, Pineda, & Rosselli, 2000; Friedman et al., 2006; Hackman, Farah, & Meaney, 2010) and therefore, have the potential to attenuate or augment the association between obesity and executive deficits. Additionally, it is possible that the effect of obesity on executive function changes across development with adolescence representing a particularly vulnerable period of development because the maturation of executive control lags behind gains in reward sensitivity (Somerville & Casey, 2010). Thus, obesity may further compromise executive abilities during adolescence, leading to a larger adverse effect of obesity on executive functioning in adolescents than in younger children. Understanding the moderating influence of developmental and demographic factors on the effect of obesity is necessary for identifying who is at risk.

The present study aims to comprehensively quantify the magnitude of impairment
in executive and reward function in pediatric obesity by conducting a meta-analysis of studies published through December 2016 that examined those cognitive functions in children under the age of 21 years without other health comorbidities. Thirty-four (50%) additional studies have been published since the previous meta-analysis, which only focused on the inhibitory control process and reward-related decision making (inclusion until July 2012; Thamotharan, Lange, Zale, Huffhines, & Fields, 2013). While a significant effect of obesity was observed on inhibition and reward related decision making, no effects were observed for attentiveness and impulsivity (Thamotharan et al., 2013). In addition to the opportunity to replicate those results, the present study extends examination to include additional executive processes, cognitive flexibility/switching and working memory. Furthermore, we examine potential sources of heterogeneity that may moderate the effect of obesity on executive and reward-related processes through sensitivity analyses examining socio-demographic factors (e.g., age and gender, SES), IQ, and study-design characteristics. Together, our meta-analysis provides the most up-to-date and comprehensive view of the status of executive and reward function in pediatric obesity.

Methods

This study followed the guidelines outlined by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (Moher, Liberati, Tetzlaff, & Altman, 2009).

Literature Search

Our search used PubMed (from 1960-2016), PsychInfo (from 1978-2016), and Academic Search Premier (from 1975-2016) and included the following search terms
attention, executive function, cognitive control, inhibition, working memory, switching, cognitive flexibility, impulsivity, delayed discounting, reward, and delay of gratification in conjunction with obesity, obese, body mass index, overweight, weight, and adiposity. Search terms for cognitive functioning were derived from common terminology related to executive and reward processes in addition to the tasks used to assess them (examples of search terms are italicized in the Introduction). The search used the limits youth, adolescents, child/children, pediatric, and human and yielded 9,677 unique studies.

Figure II-1 presents a graphic of the decision process.

Figure II-1. Flowchart Depicting Results and Methods of the Systematic Review.

Titles of studies were screened according the following exclusion criteria: (a) not written or translated to English; (b) participant age greater than 21; (c) inclusion of participants with genetic syndrome associated with obesity; (d) inclusion of participants...
diagnosed with psychopathological disorder (e.g., eating disorder or anxiety) or medical co-morbidity (e.g., metabolic syndrome or type-II diabetes); and (e) report of only latent variable for executive/reward function. Full-texts were reviewed for both the exclusion criteria and the following inclusion criteria: (a) empirical study; (b) participant sample included both participants with healthy weight and overweight/obesity; and (c) executive or reward functioning and adiposity were assessed concurrently. A total of 68 studies met criteria for inclusion, many of which assessed multiple processes of executive and reward function (Table II-1).

**Coding and Data Extraction**

All studies were coded by authors AP and CL with disagreements or errors resolved through discussion.

**Data Extraction.** Approximately half of the studies (53%, n = 36) reported means and standard deviations for obese/overweight and healthy weight groups. In the event that obese and overweight groups were reported separately, pooled means and standard deviations were used to create a single overweight/obese group. Pearson’s r was used for about a third of the studies (N = 24, 35%), with Pearson’s r derived from reported statistics for 8 studies (2: beta coefficient and standard error (SE); 2: beta coefficient and confidence interval (CI); 3: t-statistic of beta coefficient; 1: F statistic from analysis of covariance). The remaining studies reported F-statistics (N = 10: 7 main effects; 2 derived from beta coefficient and SE; 1 derived from beta coefficient and CI), proportions (N = 1), p-values (N = 1), chi-square (N = 2), and log-odds (N = 1). A total of 7 studies reported a mixture of statistical outcomes. All data was coded for the task used, the outcome measure, and whether food stimuli was used in the assessment. In addition to
Effects were categorized into one of seven cognitive process categories: (a) **Attention**: performance on individual tasks (e.g., Continuous Performance Test) or composite scores from multiple tasks involving sustained attention (e.g., Kauffman Attention Factor); (b) **Cognitive Flexibility/Switching**: performance measures such as verbal fluency, perseverative errors for the Wisconsin Card Sorting Task, and Trail Making Test B; (c) **Inhibition**: performance on response inhibition tasks such as Go-No/Go and Stop Signal Task; (d) **Interference**: performance on Flanker and Stroop interference tasks; (e) **Trait Impulsivity**: exclusively comprised of parental or self-report on questionnaires assessing impulsivity in everyday behavior (e.g., UPPS-P Impulsive Behavior Scale or Behavioral Activation Scale) – while these behaviors reflect inhibitory functioning and reward sensitivity, they were separated from the task-based response inhibition measures because they assess chronic traits; (f) **Working Memory**: performance on the span tasks requiring manipulation of information and the N-back task; (g) **Reward**: performance on delay discounting, delay of gratification, and reward-related risk taking tasks (e.g., Door Opening Task); (h) **Other**: tasks related to planning (e.g. Maze or Tower of London) or assessments of general executive functioning (e.g., Woodcock-Johnson Executive Processing). With the exception of Trait Impulsivity, all process categories had very few studies using questionnaire measures. For study and task details see Table II-1.

Further, the following study characteristics were extracted for each study: (a) sample size; (b) study design; (c) adiposity measure (i.e., BMI, skin-folds); (c) mean age
(n missing = 2) and age range of sample (n missing = 13); (d) percent of sample that was male (n missing = 1); and (e) executive measures (Table II-1).

Table II-1. Study Characteristics.

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Design</th>
<th>Adiposity Criteria</th>
<th>Mean Age (Range)</th>
<th>Gender (%M)</th>
<th>Executive Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alarcon et al. (2016)</td>
<td>152</td>
<td>Cat</td>
<td>BMI.p (&gt;85th)</td>
<td>14.1 (12 to 17)</td>
<td>56</td>
<td>Working Memory: 2-Back Task</td>
</tr>
<tr>
<td>Batterink et al. (2010)</td>
<td>35</td>
<td>Cont.</td>
<td>BMI</td>
<td>15.7 (NA)</td>
<td>0</td>
<td>Go/No-Go</td>
</tr>
<tr>
<td>Bauer et al. (2010)</td>
<td>69</td>
<td>Cat</td>
<td>BMI.p (&gt;85th)</td>
<td>16.4 (14 to 20)</td>
<td>52</td>
<td>Stroop b</td>
</tr>
<tr>
<td>Bauer et al. (2016)</td>
<td>158</td>
<td>Cat</td>
<td>BMI.p (&gt;85th)</td>
<td>15.6 (NA)</td>
<td>0</td>
<td>Attention: Sustained Attention Task</td>
</tr>
<tr>
<td>Blanco-Gomez et al. (2015)</td>
<td>424</td>
<td>Cat</td>
<td>BMI.p (&gt;95th)</td>
<td>8.5 (6 to 10)</td>
<td>49</td>
<td>Working Memory: Spatial Memory Task</td>
</tr>
<tr>
<td></td>
<td>220</td>
<td></td>
<td></td>
<td></td>
<td>56.6</td>
<td></td>
</tr>
<tr>
<td>Bonato &amp; Boland (1983a)</td>
<td>40</td>
<td>Cat</td>
<td>Triceps (&gt;1SD)</td>
<td>10.0 (8 to 11)</td>
<td>50</td>
<td>Reward: Candy and Non-Edible Choice to Wait</td>
</tr>
<tr>
<td>Bonato &amp; Boland (1983b)</td>
<td>20</td>
<td>Cat</td>
<td>Triceps (&gt;1SD)</td>
<td>10.0 (8 to 11)</td>
<td>50</td>
<td>Interference: Incompatibility (ACC &amp; RT) a</td>
</tr>
<tr>
<td>Bourget &amp; White (1984)</td>
<td>36</td>
<td>Cat</td>
<td>OW.p (&gt;110%)</td>
<td>7.14 (5 to 9)</td>
<td>0</td>
<td>Reward: Food and Toy Wait Time</td>
</tr>
<tr>
<td>Breat et al. (2007)</td>
<td>109</td>
<td>Cat</td>
<td>Adjusted BMI</td>
<td>13.4 (10 to 18)</td>
<td>45</td>
<td>Impulsivity: Matching Familiar Figure Test</td>
</tr>
<tr>
<td>Bruce et al. (2011)</td>
<td>59</td>
<td>Cont.</td>
<td>BMI.p (&gt;85th)</td>
<td>10.3 (8 to 12)</td>
<td>53</td>
<td>Reward: Points Saved</td>
</tr>
<tr>
<td>Bruce et al. (2013)</td>
<td>20</td>
<td>Cat</td>
<td>BMI</td>
<td>11.9 (10 to 14)</td>
<td>45</td>
<td>Impulsivity: Eysenck 16 Junior Questionnaire</td>
</tr>
<tr>
<td>Buck et al. (2008)</td>
<td>77</td>
<td>Cont.</td>
<td>BMI.z</td>
<td>9.3 (7 to 12)</td>
<td>55</td>
<td>Interference: Stroop Color and Word Test Children's Version</td>
</tr>
<tr>
<td>Cserjesi et al. (2007)</td>
<td>24</td>
<td>Cont.</td>
<td>BMI (&gt;24)</td>
<td>12.3 (NA)</td>
<td>100</td>
<td>Attention: 1) D2 Attention Endurance Test; 2) Digit Span Forward</td>
</tr>
<tr>
<td></td>
<td>443</td>
<td>Cont.</td>
<td>BMI.z</td>
<td>8.9 (5 to 11)</td>
<td>51</td>
<td>Switching: 1) Semantic Fluency; 2) Wisconsin Card Sorting Task (Perseverative Errors and Responses) a</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Working Memory: Digit Span Backward</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Impulsivity: Behavioral Activation Scale</td>
</tr>
</tbody>
</table>

BMI: body mass index; BMI.p: percentile; BMI.z: Z-score; BMI SDS: standardized; IOTF: International Obesity Task Force cutoffs used; Triceps: triceps skin-fold thickness; OW.p: percent overweight

a studies also included in Thamotharan et al. (2013)
b measures combined to create an aggregated effect
c interference score calculated by hand (incongruent scores - congruent scores)
<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Design</th>
<th>Adiposity Criteria</th>
<th>Mean Age (Range)</th>
<th>Gender (%M)</th>
<th>Executive Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delgado-Rico et al. (2012)</td>
<td>63</td>
<td>Cat</td>
<td>BMI</td>
<td>14.2 (12 to 17)</td>
<td>40</td>
<td>Switching: D-KEFs Stroop Switching Interference: D-KEFs Stroop Impulsivity: 1) Sensitivity to Reward; 2) UPPS-P (all subscales)</td>
</tr>
<tr>
<td>Duckworth et al. (2010)</td>
<td>105</td>
<td>Cont.</td>
<td>BMI.z</td>
<td>10.6 (NA)</td>
<td>48</td>
<td>Reward: Question Based Delay Discounting Attention: Continuous Performance Test Inhibition: Stop Signal Test Reward: Question Based Delay Discounting</td>
</tr>
<tr>
<td>Fields et al. (2011)</td>
<td>37</td>
<td>Cat</td>
<td>BMI.p (&gt;95th)</td>
<td>17.3 (14 to 19)</td>
<td>58</td>
<td>Reward: Question Based Delay Discounting Inhibition: Continuous Performance Test Reward: Door Opening Test Switching: 1) Semantic Fluency; 2) Trail Making Test B Working Memory: Digit Span Backward</td>
</tr>
<tr>
<td>Fields et al. (2013)</td>
<td>61</td>
<td>Cat</td>
<td>BMI.p (&gt;85th)</td>
<td>15.0 (14 to 16)</td>
<td>44</td>
<td>Attention: Continuous Performance Test Inhibition: Stop Signal Test Reward: Door Opening Test Switching: 1) Semantic Fluency; 2) Trail Making Test B Working Memory: Digit Span Backward</td>
</tr>
<tr>
<td>Guerrieri et al. (2007)</td>
<td>78</td>
<td>Cat</td>
<td>BMI norms</td>
<td>9.0 (8 to 10)</td>
<td>58</td>
<td>Inhibition: Stop Signal Test Reward: Door Opening Test Switching: 1) Semantic Fluency; 2) Trail Making Test B Working Memory: Digit Span Backward</td>
</tr>
<tr>
<td>Hjorth et al. (2016)</td>
<td>744</td>
<td>Cat</td>
<td>BMI.p (&gt;85th)</td>
<td>9.9 (9 to 11)</td>
<td>51</td>
<td>Attention: 1) D2 Attention Endurance Test Impulsivity: Barratt Impulsiveness Scale-15 Interference: Flanker (ACC &amp; RT)</td>
</tr>
<tr>
<td>Hofmann et al. (2015)</td>
<td>58</td>
<td>Cat</td>
<td>BMI.p (&gt;97th)</td>
<td>13.6 (10 to 18)</td>
<td>59</td>
<td>Inhibition: Stop Signal Test Reward: Door Opening Test Switching: 1) Semantic Fluency; 2) Trail Making Test B Working Memory: Digit Span Backward</td>
</tr>
<tr>
<td>Huang et al. (2015)</td>
<td>525</td>
<td>Cont.</td>
<td>BMI</td>
<td>13.0 (NA)</td>
<td>48</td>
<td>Inhibition: Children's Behavior Questionnaire-Effortful Control Reward: Food and Gift Delay of Gratification</td>
</tr>
<tr>
<td>Hughes et al. (2015)</td>
<td>187</td>
<td>Cont.</td>
<td>BMI.z</td>
<td>4.8 (NA)</td>
<td>52</td>
<td>Inhibition: Children's Behavior Questionnaire-Effortful Control Reward: Food and Gift Delay of Gratification</td>
</tr>
<tr>
<td>Johnson et al. (1978)</td>
<td>142</td>
<td>Cont.</td>
<td>Skinfold</td>
<td>8.6 (6 to 11)</td>
<td>45</td>
<td>Reward: Food and Toy Items Delayed Inhibition: Stop Signal Test Reward: Door Opening Test Switching: 1) Semantic Fluency; 2) Trail Making Test B Working Memory: Digit Span Backward</td>
</tr>
<tr>
<td>Kamijo et al. (2012a)</td>
<td>126</td>
<td>Cat</td>
<td>BMI.p (&gt;85th)</td>
<td>8.9 (7 to 9)</td>
<td>50</td>
<td>Inhibition: Go/No-Go Inhibition: Stop Signal Test Reward: Door Opening Test Switching: 1) Semantic Fluency; 2) Trail Making Test B Working Memory: Digit Span Backward</td>
</tr>
<tr>
<td>Kamijo et al. (2012b)</td>
<td>74</td>
<td>Cat</td>
<td>BMI.p (&gt;95th)</td>
<td>9.0 (NA)</td>
<td>49</td>
<td>Inhibition: Go/No-Go Inhibition: Stop Signal Test Reward: Door Opening Test Switching: 1) Semantic Fluency; 2) Trail Making Test B Working Memory: Digit Span Backward</td>
</tr>
<tr>
<td>Kamijo et al. (2014)</td>
<td>74</td>
<td>Cat</td>
<td>BMI.p (&gt;95th)</td>
<td>8.9 (7.9 to 9.9)</td>
<td>54</td>
<td>Inhibition: Flanker Inhibition: Stop Signal Test Reward: Door Opening Test Switching: 1) Semantic Fluency; 2) Trail Making Test B Working Memory: Digit Span Backward</td>
</tr>
<tr>
<td>Kulendran et al. (2014)</td>
<td>103</td>
<td>Cat</td>
<td>BMI.p (&gt;85th)</td>
<td>14.3 (10 to 17)</td>
<td>38</td>
<td>Inhibition: Stop Signal Test (SSRT, SSD, errors)</td>
</tr>
<tr>
<td>Levitian et al. (2015)</td>
<td>193</td>
<td>Cont.</td>
<td>BMI.z</td>
<td>4.0 (NA)</td>
<td>53</td>
<td>Inhibition: Stop Signal Test</td>
</tr>
</tbody>
</table>

Note: value in parentheses after adiposity measure indicate cutoff used to identify overweight/obesity
BMI: body mass index; BMI.p: percentile; BMI.z: Z-score; BMI SDS: standardized; IOTF: International Obesity Task Force cutoffs used; Triceps: triceps skin-fold thickness; OW.p: percent overweight studies also included in Thamotharan et al. (2013) measures combined to create an aggregated effect interference score calculated by hand (incongruent scores - congruent scores)
<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Design</th>
<th>Adiposity Criteria</th>
<th>Mean Age (Range)</th>
<th>Gender (%M)</th>
<th>Executive Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Li et al. (2008)</td>
<td>2519</td>
<td>Cont.</td>
<td>BMI.p (&gt;85th)</td>
<td>12.0 (8 to 16)</td>
<td>52</td>
<td>Working Memory: Digit Span Backward</td>
</tr>
<tr>
<td>Lu et al. (2014)</td>
<td>87</td>
<td>Cont.</td>
<td>BMI</td>
<td>12.7 (NA)</td>
<td>55</td>
<td>Reward: Delay Discounting Task</td>
</tr>
<tr>
<td>Maayan et al. (2011)</td>
<td>91</td>
<td>Cat</td>
<td>BMI.p (&gt;95th)</td>
<td>17.4 (14 to 21)</td>
<td>39</td>
<td>Attention: 1) WRAML index; 2) Trail Making Test A Switching: Trail Making Test B Interference: Stroop Color Word Number Correct Working Memory: WRAML index</td>
</tr>
<tr>
<td>Mata et al. (2015)</td>
<td>54</td>
<td>Cat</td>
<td>BMI (IOTF)</td>
<td>15.4 (12 to 18)</td>
<td>39</td>
<td>Reward: Risk Gains Task</td>
</tr>
<tr>
<td>Matton et al. (2013)</td>
<td>579</td>
<td>Cont.</td>
<td>Adjusted BMI</td>
<td>15.7 (14 to 19)</td>
<td>40</td>
<td>Impulsivity: Sensitivity to Reward (SRSPQ &amp; Behavioral Activation System)³ Impulsivity: Barratt Impulsiveness Scale² Reward: Food⁴ and Toy⁵ Delay of Gratification</td>
</tr>
<tr>
<td>Meule et al. (2016)</td>
<td>122</td>
<td>Cont.</td>
<td>BMI</td>
<td>13.6 (10 to 18)</td>
<td>48</td>
<td>Working Memory: Sentences Interference: D-KEFs Stroop Impulsivity: 1) SPSRQ; 2) UPPS-P (all subscales)³ Impulsivity: Behavioral Activation Scale⁴ Inhibition: Stop Signal Task Reward: Door Opening Task Inhibition: Stop Signal Task Food and Toy Other: Woodcock-Johnson III Executive Processing Attention: 1) Kauffman Attention Factor; 2) SDAG</td>
</tr>
<tr>
<td>A. L. Miller et al. (2016)</td>
<td>133</td>
<td>Cont.</td>
<td>BMI.p</td>
<td>2.8 (NA)</td>
<td>50</td>
<td>Impulsivity: Behavioral Activation Scale⁴ Inhibition: Stop Signal Task Reward: Door Opening Task Inhibition: Stop Signal Task Food and Toy Other: Woodcock-Johnson III Executive Processing Attention: 1) Kauffman Attention Factor; 2) SDAG</td>
</tr>
<tr>
<td>Mond et al. (2007)</td>
<td>9415</td>
<td>Cont.</td>
<td>BMI (IOTF)</td>
<td>6.0 (4 to 8)</td>
<td>52</td>
<td>Working Memory: Sentences Interference: D-KEFs Stroop Impulsivity: 1) SPSRQ; 2) UPPS-P (all subscales)³ Impulsivity: Behavioral Activation Scale⁴ Inhibition: Stop Signal Task Reward: Door Opening Task Inhibition: Stop Signal Task Food and Toy Other: Woodcock-Johnson III Executive Processing Attention: 1) Kauffman Attention Factor; 2) SDAG</td>
</tr>
<tr>
<td>Moreno-Lopez et al. (2012)</td>
<td>52</td>
<td>Cat</td>
<td>BMI (IOTF)</td>
<td>14.2 (12 to 17)</td>
<td>33</td>
<td>Impulsivity: Behavioral Activation Scale⁴ Inhibition: Stop Signal Task Reward: Door Opening Task Inhibition: Stop Signal Task Food and Toy Other: Woodcock-Johnson III Executive Processing Attention: 1) Kauffman Attention Factor; 2) SDAG</td>
</tr>
<tr>
<td>Nederkoorn et al. (2006)</td>
<td>63</td>
<td>Cat</td>
<td>BMI</td>
<td>13.7 (12 to 15)</td>
<td>40</td>
<td>Impulsivity: Behavioral Activation Scale⁴ Inhibition: Stop Signal Task Reward: Door Opening Task Inhibition: Stop Signal Task Food and Toy Other: Woodcock-Johnson III Executive Processing Attention: 1) Kauffman Attention Factor; 2) SDAG</td>
</tr>
<tr>
<td>Nederkoorn et al. (2007)</td>
<td>26</td>
<td>Cont.</td>
<td>OW.p (&gt;120%)</td>
<td>9.3 (NA)</td>
<td>35</td>
<td>Inhibition: Stop Signal Task Reward: Door Opening Task Inhibition: Stop Signal Task Food and Toy Other: Woodcock-Johnson III Executive Processing Attention: 1) Kauffman Attention Factor; 2) SDAG</td>
</tr>
<tr>
<td>Nederkoorn et al. (2012)</td>
<td>89</td>
<td>Cat</td>
<td>OW.p (&gt;120%)</td>
<td>8.1 (7 to 9)</td>
<td>45</td>
<td>Inhibition: Stop Signal Task Reward: Door Opening Task Inhibition: Stop Signal Task Food and Toy Other: Woodcock-Johnson III Executive Processing Attention: 1) Kauffman Attention Factor; 2) SDAG</td>
</tr>
<tr>
<td>Niemiro et al. (2016)</td>
<td>28</td>
<td>Cat</td>
<td>BMI.p (&gt;85th)</td>
<td>8.9 (8 to 10)</td>
<td>100</td>
<td>Other: Woodcock-Johnson III Executive Processing Attention: 1) Kauffman Attention Factor; 2) SDAG</td>
</tr>
<tr>
<td>Parisi et al. (2010)</td>
<td>318</td>
<td>Cat</td>
<td>BMI.p (&gt;85th)</td>
<td>9.9 (6 to 13)</td>
<td>46.9</td>
<td>Attention: 1) Kauffman Attention Factor; 2) SDAG</td>
</tr>
<tr>
<td>Pauli-Pott et al. (2010)</td>
<td>111</td>
<td>Cont.</td>
<td>BMI SDS</td>
<td>11.1 (7 to 15)</td>
<td>43</td>
<td>Attention: TAP</td>
</tr>
<tr>
<td>Pearce et al. (submitted)</td>
<td>59</td>
<td>Cat</td>
<td>BMI.p (&gt;95th)</td>
<td>11.7 (7 to 18)</td>
<td>41</td>
<td>Attention: 1-Back Task Inhibition: Stop Signal Task (SSRT &amp; SSD)³ Reward: BART (Pops and Pumps)⁴ Working Memory: 2-Back Task Switching: BRIEF Switch Inhibition: BRIEF (Inhibit &amp; Emotional Control subscales)³ Working Memory: BRIEF Other: BRIEF (Initiate, Plan and Organization, Organization of Materials, &amp; Monitoring subscales)³</td>
</tr>
</tbody>
</table>

Note: value in parentheses after adiposity measure indicate cutoff used to identify overweight/obesity
BMI: body mass index; BMI.p: percentile; BMI.z: Z-score; BMI SDS: standardized; IOTF: International Obesity Task Force cutoffs used; Triceps: triceps skin-fold thickness; OW.p: percent overweight
³studies also included in Thamotharan et al. (2013)
²measures combined to create an aggregated effect
³interference score calculated by hand (incongruent scores - congruent scores)
<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Design</th>
<th>Adiposity Criteria</th>
<th>Mean Age (Range)</th>
<th>Gender (%M)</th>
<th>Executive Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pontifex et al. (2014)</td>
<td>204</td>
<td>Cont.</td>
<td>Total Fat</td>
<td>8.8 (7 to 10)</td>
<td>53</td>
<td>Switching: Switch Task (Heterogeneous and Homogeneous)^&lt;sub&gt;a&lt;/sub&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Interference: Flanker</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Switching: Trail Making Test B-A</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Interference: Stroop</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Interference</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Working memory: 1) WISC Index; 2) Letter-Number Sequencing</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Other: 1) Category Test; 2) Tower of London</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Reward: 1) Iowa Gambling Task; 2) Risky Choices (Dice and Cup Tasks)</td>
</tr>
<tr>
<td>Ross et al. (2015)</td>
<td>130</td>
<td>Cat</td>
<td>BMI (&gt;30)</td>
<td>19.5 (15 to 21)</td>
<td>42</td>
<td>Switching: Trail Making Test B-A</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Interference: Flanker</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Working memory: 1) WISC Index; 2) Letter-Number Sequencing</td>
</tr>
<tr>
<td>Scholten et al. (2014)</td>
<td>1377</td>
<td>Cat</td>
<td>BMI.z</td>
<td>10.2 (8 to 12)</td>
<td>51</td>
<td>Impulsivity: Temperament in Middle Childhood Questionnaire</td>
</tr>
<tr>
<td>Schwartz et al. (2013)</td>
<td>983</td>
<td>Cont.</td>
<td>Visceral Fat</td>
<td>15.0 (12 to 18)</td>
<td>49</td>
<td>Reward: Door Opening Task</td>
</tr>
<tr>
<td>Sigal &amp; Adler (1976)</td>
<td>64</td>
<td>Cat</td>
<td>OW.p (&gt;125%)</td>
<td>NA (8 to 13)</td>
<td>100</td>
<td>Reward: Food and Non-Food Weight Time</td>
</tr>
<tr>
<td>Skoranski et al. (2013)</td>
<td>60</td>
<td>Cat</td>
<td>BMI.p (&gt;85th)</td>
<td>12.8 (7 to 17)</td>
<td>38</td>
<td>Interference: Simon&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Sobhany &amp; Rogers (1985)</td>
<td>112</td>
<td>Cat</td>
<td>Triceps (&gt;90th)</td>
<td>4.8 (3 to 5)</td>
<td>49</td>
<td>Reward: Food and non-Food Choice to Wait</td>
</tr>
<tr>
<td></td>
<td>134</td>
<td></td>
<td></td>
<td>8.6 (6 to 13)</td>
<td>49</td>
<td>Reward: Food and non-Food Choice to Wait</td>
</tr>
<tr>
<td>van den Berg et al. (2011)</td>
<td>331</td>
<td>Cat</td>
<td>BMI SDS</td>
<td>9.1 (6 to 13)</td>
<td>55.3</td>
<td>Impulsivity: SRSPQ</td>
</tr>
<tr>
<td>Velders et al. (2012)</td>
<td>1621</td>
<td>Cont.</td>
<td>BMI SDS</td>
<td>4.0 (NA)</td>
<td>51</td>
<td>Switching: BRIEF Switch</td>
</tr>
<tr>
<td>Verbeken et al. (2009)</td>
<td>82</td>
<td>Cat</td>
<td>Adjusted BMI</td>
<td>11.8 (10 to 14)</td>
<td>40</td>
<td>Interference: Test of Everyday Attention for Children-Opposite Worlds</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Inhibition: Stop Signal Task</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Reward: 1) Maudsley Index of Childhood Delay Aversion; 2) Door Opening Task</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Other: Five Digit Test Circle Drawing</td>
</tr>
<tr>
<td>Verbeken et al. (2012)</td>
<td>438</td>
<td>Cont.</td>
<td>Adjusted BMI</td>
<td>12.0 (10 to 15)</td>
<td>47.5</td>
<td>Reward: Behavioral Activation Scale Drive</td>
</tr>
<tr>
<td>Verbeken et al. (2014)</td>
<td>132</td>
<td>Cont.</td>
<td>BMI.p (&gt;85th)</td>
<td>12.4 (11 to 16)</td>
<td>45.5</td>
<td>Reward: Hungry Donkey Task</td>
</tr>
</tbody>
</table>

Note: value in parentheses after adiposity measure indicate cutoff used to identify overweight/obesity
BMI: body mass index; BMI.p: percentile; BMI.z: Z-score; BMI SDS: standardized; IOTF: International Obesity Task Force cutoffs used; Triceps: triceps skin-fold thickness; OW.p: percent overweight
<sup>a</sup>studies also included in Thamotharan et al. (2013)
<sup>b</sup>measures combined to create an aggregated effect
<sup>c</sup>interference score calculated by hand (incongruent scores - congruent scores)
Table II-1 (Continued).

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Design</th>
<th>Adiposity Criteria</th>
<th>Mean Age (Range)</th>
<th>Gender (%M)</th>
<th>Executive Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verdejo-Garcia et al. (2010)</td>
<td>61</td>
<td>Cat</td>
<td>BMI (IOTF)</td>
<td>14.9 (13 to 16)</td>
<td>61</td>
<td>Switching: 1) Trail Making Test B-A; 2) Five Digit Test Interference: 1) Stroop; 2) Five Digit Test Impulsivity: 1) SPSRQ; 2) UPPS-P (all subscales) Reward: 1) Delay Discounting; 2) Iowa Gambling Task Working Memory: Letter-Number Sequencing</td>
</tr>
<tr>
<td>Verdejo-Garcia et al. (2014)</td>
<td>80</td>
<td>Cat</td>
<td>BMI (IOTF)</td>
<td>15.2 (12 to 18)</td>
<td>39</td>
<td>Reward: SRSPQ Inhibition: TAP Go/No-Go (total and errors)</td>
</tr>
<tr>
<td>Wirt et al. (2014)</td>
<td>496</td>
<td>Cat</td>
<td>BMI.p (&gt;90th)</td>
<td>7.0 (5 to 9)</td>
<td>49.8</td>
<td>Attention: TAP Switching: TAP Inhibition: TAP Go/No-Go</td>
</tr>
<tr>
<td>Wirt et al. (2015)</td>
<td>445</td>
<td>Cont.</td>
<td>BMI.p (&gt;90th)</td>
<td>7.0 (5 to 9)</td>
<td>49.8</td>
<td>Switching: 1) Trail Making Test B; 2) Wisconsin Card Sorting Task Perseverative Errors Interference: Stroop Working Memory: WRAML index</td>
</tr>
<tr>
<td>Yau et al. (2014)</td>
<td>60</td>
<td>Cat</td>
<td>BMI.p (&gt;95th)</td>
<td>17.4 (14 to 20)</td>
<td>40</td>
<td>Attention: Continuous Performance Test Working Memory: Letter N-Back Other: Penn Conditional Exclusion Task</td>
</tr>
<tr>
<td>Zamzow et al. (2014)</td>
<td>2841</td>
<td>Cat</td>
<td>BMI</td>
<td>NA (8 to 19)</td>
<td>NA</td>
<td>Attention: Continuous Performance Test Working Memory: Letter N-Back Other: Penn Conditional Exclusion Task</td>
</tr>
</tbody>
</table>

Note: value in parentheses after adiposity measure indicate cutoff used to identify overweight/obesity
BMI: body mass index; BMI.p: percentile; BMI.z: Z-score; BMI SDS: standardized; IOTF: International Obesity Task Force cutoffs used; Triceps: triceps skin-fold thickness; OW.p: percent overweight
^studies also included in Thamotharan et al. (2013)
^a measures combined to create an aggregated effect
^b interference score calculated by hand (incongruent scores - congruent scores)

Data Analysis

All data analysis was completed using R (R Core Team, 2014). Study results were converted to Hedge’s g (Del Re, 2013), which adjusts for the positive bias seen in Cohen’s d (Hedges, 1982). Negative effects indicate worse performance in the obese/overweight group or with greater adiposity. When multiple outcome measures were reported for a single task, a combined weighted mean effect size and standard error was computed to account for the degree of dependency of within-study aggregation.

Results derived from a composite of multiple tasks were included only if: (a) the
composite was derived through standard or statistical procedure (e.g., principal component analysis); or (b) composite reflected a single executive process consistent with the process categories listed earlier.

**Statistical Model.** Random effect models using a restricted maximum-likelihood estimator and inverse variance weights were used to estimate the effect of obesity on executive and reward function overall and for each component processes model (Viechtbauer, 2010). Sensitivity analyses were completed using mixed effects meta-regression models for the following socio-demographic and study/task characteristics: (a) Mean age of the sample; (b) Gender composition of the sample (percent male); (c) the effect of adiposity on IQ (Hedge’s g estimate); and (d) the effect of adiposity on SES (Hedge’s g estimate); (e) Study Design, which was coded as continuous for studies assessing correlation with adiposity and categorical for studies assessing adiposity through group differences; (f) Task Category, which was included when clusters of studies used the same or similar tasks and was included for Cognitive Flexibility/Switching, Inhibition, Interference, Working Memory, and Reward-Related Decision Making models; and (g) Food Stimuli, which was included for Delay of Gratification tasks that characterized the delayed rewards as food versus non-food.

**Heterogeneity.** Although Cochrane’s Q, which allows for null-hypothesis testing for violation of homogeneity across studies, and the I² statistic, which estimates the proportion of variance in true effects relative to observed variance, are commonly used to classify heterogeneity, both have been shown to increase with increasing number of studies in the model and size of studies in the model (Alba et al., 2016; Ruecker, Schwarzer, Carpenter, & Schumacher, 2008). In contrast, τ², which reflects between
study variance derived from random intercept models, does not systematically vary with
either number of studies or size of studies in the model. Thus, \( \tau^2 \) was used to quantify
heterogeneity by calculating prediction intervals, which estimate the variability of the
ture effect of obesity (Borenstein, Higgins, Hedges, & Rothstein, 2017; Riley, Higgins, &
Deeks, 2011).

**Publication Bias.** Publication bias was assessed through funnel plot asymmetry
and the fail-safe N (FSN). Funnel plots were created using standard errors and tested for
asymmetry using Egger’s regression test (Egger, Smith, Schneider, & Minder, 1997).
However, in the presence of heterogeneity, caution was taken when interpreting funnel
plot asymmetry because asymmetry may be attributable to methodological differences in
studies, true heterogeneity due to differences in study characteristics, or artifact due to
sampling variation in addition to publication bias (Sterne et al., 2011; Terrin, Schmid,
Lau, & Olkin, 2003). A weighted FSN was also used to assess number of unpublished,
un-sampled, or novel null findings required to make the combined effect non-significant
(i.e., the file door problem). The FSN does not test for publication bias, but rather
represents a way to interpret the stability of the finding such that a FSN greater than 5k +
10 (k: number of effects in model) represents a high tolerance to unpublished null
findings (Rosenthal, 1979).

**Results**

A total of 70 unique samples, extracted from 68 studies, were used in these
analyses. Twenty of the 68 studies were also included by the previous meta-analysis
(Thamotharan et al., 2013) while 3 studies included in that paper were excluded due to
meeting our exclusion criteria (report of only latent variables, medical co-morbidities, or
existing conditions). The number of effects sizes extracted from each study ranged from 1 to 14 while study samples sizes ranged from 20 to 9,415 participants (Table II-2).

Table II-2. Model Characteristics.

<table>
<thead>
<tr>
<th>Model</th>
<th>Age</th>
<th>Gender (%M)</th>
<th>Studies Included</th>
<th>Effects Included</th>
<th>Participants</th>
<th>Sample&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Executive Composite</td>
<td>11.3</td>
<td>48.1</td>
<td>70</td>
<td>149</td>
<td>30,359</td>
<td>57,800</td>
</tr>
<tr>
<td>Attention</td>
<td>12.1</td>
<td>46.6</td>
<td>12</td>
<td>15</td>
<td>6,259</td>
<td>6,692</td>
</tr>
<tr>
<td>Switching</td>
<td>12.3</td>
<td>52.5</td>
<td>14</td>
<td>19</td>
<td>6,137</td>
<td>7,157</td>
</tr>
<tr>
<td>Inhibition</td>
<td>9.7</td>
<td>44.8</td>
<td>18</td>
<td>19</td>
<td>4,070</td>
<td>4,159</td>
</tr>
<tr>
<td>Interference</td>
<td>13.2</td>
<td>46.4</td>
<td>16</td>
<td>17</td>
<td>4,208</td>
<td>4,269</td>
</tr>
<tr>
<td>Impulsivity</td>
<td>12.8</td>
<td>43.9</td>
<td>17</td>
<td>20</td>
<td>4,160</td>
<td>4,326</td>
</tr>
<tr>
<td>Working Memory</td>
<td>13.5</td>
<td>48.9</td>
<td>15</td>
<td>17</td>
<td>18,713</td>
<td>19,826</td>
</tr>
<tr>
<td>Reward</td>
<td>11</td>
<td>49.1</td>
<td>25</td>
<td>36</td>
<td>5,268</td>
<td>8,048</td>
</tr>
</tbody>
</table>

Note: The Overall model contains all executive process and reward models in addition to studies falling in the Other category (Studies = 6; Participants = 3,323)
<sup>a</sup>Total sample size for models counts multiple measures from same study separately

Table II-3. Model Results.

<table>
<thead>
<tr>
<th>Model</th>
<th>Model Statistics</th>
<th>Heterogeneity Estimates</th>
<th>Model Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>k</td>
<td>β (95% CI)</td>
<td>Z</td>
</tr>
<tr>
<td>Demographic Models</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IQ</td>
<td>15</td>
<td>-0.30 (-0.51, -0.09)</td>
<td>-2.79</td>
</tr>
<tr>
<td>SES</td>
<td>25</td>
<td>-0.39 (-0.57, -0.20)</td>
<td>-4.05</td>
</tr>
<tr>
<td>Executive Models</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall Model</td>
<td>149</td>
<td>-0.24 (-0.30, -0.19)</td>
<td>-8.43</td>
</tr>
<tr>
<td>Attention</td>
<td>15</td>
<td>-0.19 (-0.30, -0.08)</td>
<td>-3.29</td>
</tr>
<tr>
<td>Switching</td>
<td>19</td>
<td>-0.21 (-0.32, -0.11)</td>
<td>-4.12</td>
</tr>
<tr>
<td>Inhibition</td>
<td>19</td>
<td>-0.39 (-0.51, -0.26)</td>
<td>-6.10</td>
</tr>
<tr>
<td>Interference</td>
<td>17</td>
<td>-0.28 (-0.50, -0.05)</td>
<td>-2.38</td>
</tr>
<tr>
<td>Trait Impulsivity</td>
<td>20</td>
<td>-0.06 (-0.18, 0.07)</td>
<td>-0.94</td>
</tr>
<tr>
<td>Working Memory</td>
<td>17</td>
<td>-0.20 (-0.32, -0.07)</td>
<td>-3.13</td>
</tr>
<tr>
<td>Reward</td>
<td>36</td>
<td>-0.25 (-0.36, -0.15)</td>
<td>-4.86</td>
</tr>
<tr>
<td>Delay of Gratification</td>
<td>18</td>
<td>-0.25 (-0.36, -0.13)</td>
<td>-4.29</td>
</tr>
</tbody>
</table>

CI: Confidence Interval; FSN: Fail-Safe N; PI: Prediction Interval; *<i>p </i>< 0.05; **<i>p </i>< 0.01; ***<i>p </i>< 0.001

Random Intercept Models (Table II-3)

**IQ and SES.** A total of 15 studies (22%) reported data on intelligence, while 25 (37%) reported data for SES. Adiposity had a significant small negative effect for IQ and SES. Both models showed wide prediction intervals indicating non-trivial heterogeneity,
however, there was no funnel plot asymmetry and both models showed the FSN’s above Rosenthal’s (1979) cutoff for high tolerance of unpublished null findings. Together, these models indicate that greater adiposity was associated with lower intelligence and lower SES, however, the breadth of the prediction interval indicates that the true effect varies substantially, likely partially due to differences in measurement and sample characteristics.

**Overall and Component Process Models.** There was a significant small negative effect of obesity in the Overall model, indicating worse functioning in children and adolescents with obesity, regardless of component process. Given the heterogeneity seen in the wide prediction interval, the significant funnel plot asymmetry may not reflect true publication bias but rather systematic heterogeneity across studies, such as cognitive process assessed. The FSN far exceeded the Rosenthal’s (1979) cut off indicating that the model was robust to potential unpublished or null findings. A sensitivity test using a factor containing all component processes (i.e., Attention, Cognitive Flexibility/Switching, Inhibition, Interference, Impulsivity, Working Memory, Reward-Related Decision Making, and Other) was conducted to determine if component processes differ in the size of the effect of obesity. Note that Delay of Gratification was not included in this variable because it represents a subset of studies included within Reward-Related Decision Making. This model showed a marginally significant main effect ($Q_{\text{moderator}}(7) = 13.28, p = 0.067$) with uncorrected post-hoc comparisons indicating that the effect of adiposity was more negative for Inhibition ($\beta=-0.36, \text{SE}=0.11, p = 0.001$) and Reward-Related Decision Making ($\beta=-0.25, \text{SE}=0.10, p = 0.010$) than for Trait Impulsivity. Trend level differences also suggested more negative effects for
Cognitive Flexibility/Switching ($\beta=-0.19$, SE=0.11, $p = 0.077$) and Interference ($\beta=-0.21$, SE=0.12, $p = 0.066$) than for Impulsivity and more negative effects for Inhibition than for Working Memory ($\beta=-0.19$, SE=0.11 $p = 0.092$).

In light of evidence for possible differences in the effect of obesity by component process, separate models were used to assess specific effects of pediatric obesity. Given too few studies, the “Other” category was not examined in a separate model. All processes except Trait Impulsivity showed small negative effects of adiposity, indicating that greater adiposity was associated with worse functioning. Thus, Trait Impulsivity was not included in further analyses. Prediction intervals for Attention, Cognitive Flexibility/Switching, and Inhibition show a distribution of true effects that range from large and moderate negative effects of obesity to negligible positive effects. Interference, Reward-Related Decision Making, and Working Memory, however, had prediction intervals that extended into small and moderate positive effects. Attention, Cognitive Flexibility/Switching, Inhibition, Working Memory, and Reward-Related Decision Making all showed evidence of funnel plot asymmetry, however, heterogeneity seen in the prediction intervals indicate there may be study-level differences driving the asymmetry. The majority of the models were robust to potentially unknown null data with only Working Memory and Delay of Gratification showing FSN values that did not meet Rosenthal’s (1979) cutoff, indicating that new or unpublished null results may affect the strength of the effect of adiposity on those processes. In sum, these models provide evidence for three important findings: first, pediatric obesity is associated with an overall executive and reward-related deficit; second, pediatric obesity has a significant negative effect on all component processes except Trait Impulsivity; and third, the
prediction intervals indicate that although the effect of pediatric obesity was negative, there may be important differences across studies that influence this effect.

**Sensitivity Analyses** (Table II-4)

Socio-demographic and study/task design characteristics were independently examined in order to determine whether they moderated the observed significant negative effects of obesity.

**Attention.** A marginally significant effect of Age indicated that higher mean sample age was associated with more negative effects of adiposity (Figure II-2A). Thus, deficits in attention increased for samples with older children with obesity. No other moderators were significant.

**Inhibition.** A significant effect of Age indicated that higher mean sample age was associated with more negative effects of adiposity (Figure II-2B). Additionally, a significant effect of Gender indicated that a higher composition of females in a sample was associated with more negative effects of adiposity (Figure II-2C). Although Study Design was not significant, there was an effect of Task Design ($Q_{\text{moderator}}(2) = 37.27, p < 0.001$). Studies assessing response inhibition with performance measures (Go/No-Go task: $n = 5; \beta = -0.32, SE = 0.08, p < 0.001$ and stop signal task: $n = 10; \beta = -0.47, SE = 0.08, p < 0.001$; no difference between tasks, $p = 0.129$) showed greater negative effects of adiposity than questionnaire-based assessments (Figure II-2D). Together, these results indicate that older children and females were more vulnerable to the negative effects of obesity and that task performance was more sensitive to the effect of obesity on inhibition than behavioral reports. No other moderators were significant.
Table II-4. Sensitivity Results.

<table>
<thead>
<tr>
<th></th>
<th>Model Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>k</td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>Overall Model 145</td>
<td>-0.001 (-0.02, 0.01)</td>
</tr>
<tr>
<td>Attention</td>
<td>14</td>
</tr>
<tr>
<td>Switching</td>
<td>19</td>
</tr>
<tr>
<td>Inhibition</td>
<td>19</td>
</tr>
<tr>
<td>Interference</td>
<td>17</td>
</tr>
<tr>
<td>Working Memory</td>
<td>16</td>
</tr>
<tr>
<td>Reward</td>
<td>35</td>
</tr>
<tr>
<td>Gender (% Male)</td>
<td></td>
</tr>
<tr>
<td>Overall Model 146</td>
<td>-0.002 (-0.01, 0.003)</td>
</tr>
<tr>
<td>Attention</td>
<td>14</td>
</tr>
<tr>
<td>Switching</td>
<td>19</td>
</tr>
<tr>
<td>Inhibition</td>
<td>19</td>
</tr>
<tr>
<td>Interference</td>
<td>17</td>
</tr>
<tr>
<td>Working Memory</td>
<td>16</td>
</tr>
<tr>
<td>Reward</td>
<td>36</td>
</tr>
<tr>
<td>Study Design a</td>
<td></td>
</tr>
<tr>
<td>Overall Model 149</td>
<td>-0.06 (-0.18, 0.05)</td>
</tr>
<tr>
<td>Attention</td>
<td>15</td>
</tr>
<tr>
<td>Switching</td>
<td>19</td>
</tr>
<tr>
<td>Inhibition</td>
<td>19</td>
</tr>
<tr>
<td>Interference</td>
<td>17</td>
</tr>
<tr>
<td>Working Memory</td>
<td>17</td>
</tr>
<tr>
<td>Reward</td>
<td>36</td>
</tr>
<tr>
<td>Food Stimuli c</td>
<td></td>
</tr>
<tr>
<td>Delay of Gratification</td>
<td>18</td>
</tr>
<tr>
<td>IQ</td>
<td></td>
</tr>
<tr>
<td>Overall Model 45</td>
<td>-0.01 (-0.31, 0.29)</td>
</tr>
<tr>
<td>Attention</td>
<td>8</td>
</tr>
<tr>
<td>Switching</td>
<td>9</td>
</tr>
<tr>
<td>Interference</td>
<td>7</td>
</tr>
<tr>
<td>Working Memory</td>
<td>8</td>
</tr>
<tr>
<td>SES</td>
<td></td>
</tr>
<tr>
<td>Overall Model 58</td>
<td>-0.09 (-0.31, 0.13)</td>
</tr>
<tr>
<td>Attention</td>
<td>6</td>
</tr>
<tr>
<td>Switching</td>
<td>10</td>
</tr>
<tr>
<td>Inhibition</td>
<td>9</td>
</tr>
<tr>
<td>Interference</td>
<td>8</td>
</tr>
<tr>
<td>Working Memory</td>
<td>7</td>
</tr>
<tr>
<td>Reward</td>
<td>6</td>
</tr>
</tbody>
</table>

$p < 0.10; \ast p < 0.05; \ast\ast p < 0.01; \ast\ast\ast p < 0.001$

a: Cochrane's residual Q; degrees of freedom = k-p (k=number of studies; p=number of model parameters, including intercept)
b: reference level is continuous design
c: reference level is no food stimuli
**Working Memory.** A significant effect of Study Design indicated that adiposity as a categorical, rather than continuous, variable showed more negative effects of adiposity (Figure II-2E). No other moderators were significant, including task differences (span-based versus miscellaneous tasks; \( p = 0.158 \)).

**Remaining Models.** None of the socio-demographic or study design characteristics were significant for the following models: Overall, Cognitive Flexibility/Switching, Interference, Reward-Related Decision Making, and Delay of Gratification. Similarly, there were no differences by Task Category in models for Cognitive Flexibility/Switching (trail-making test versus fluency or questionnaire measures; \( p = 0.102 \)), Interference (Color-Word Stroop versus Flanker or Simon tasks versus miscellaneous tasks; \( p = 0.690 \)), nor Reward-Related Decision Making (delay of gratification versus risk-taking tasks versus delay discounting/aversion; \( p = 0.147 \)). Additionally, there was no effect of Food Stimuli for Delay of Gratification (\( p = 0.411 \)) indicating that food rewards did not carry a unique effect of obesity on Reward-Related Decision Making compared to non-food rewards.

**Discussion**

Small-to-moderate deleterious effects of obesity were observed on executive and reward-related performance but not on reported impulsivity, with larger effects on inhibitory task performance in older and predominantly female samples. Although obesity was associated with lower IQ and SES, these variables did not predict the observed effects. Together, these findings replicate and extend findings from the previous meta-analysis (Thamotharan et al., 2013) by including additional executive processes and evaluating the moderating role of demographic variables and study/task characteristics.
The results suggest cognitive and demographic intervention targets for prevention and mitigation of obesogenic behavior.

**Figure II-2.** These plots depict significant moderators of the effect of obesity on **executive abilities**. The size of the points on the graphs related to the contribution or weight of that study in the model. The dotted lines reflect predicted marginal effects with 95% confidence intervals.
The present findings provide a comprehensive view of the current status of the effect of pediatric obesity on executive and reward functioning. Our findings replicate those from Thamotharan et al (2013) by showing negative effects of obesity on inhibitory control and reward-related decision making but no effect of obesity on parental/self-report measures of impulsivity. These differences were not due to insensitivity of questionnaire measures because reward functions such as delay of gratification showed a significant effect of obesity despite inclusion of some parental/self-report measures. Beyond replication, our findings showed negative effects of obesity on other component processes including working memory and cognitive flexibility/shifting. Additionally, the effect of obesity on attention was significant in the present study but not in Thamotharan et al. (2013), perhaps due to increased power after including the 7 studies published since 2012. Despite replication, the present effect sizes were slightly smaller than those from Thamotharan et al (2013), potentially due to the inclusion of double the number of included studies, studies examining a wider range of executive functions, or the strict exclusion of samples with medical comorbidities. Nevertheless, the largely consistent findings across these two meta-analyses underscore the stability of deficits for inhibitory and reward function, and therefore, their importance in mediating behaviors that promote obesity in children and adolescents.

Sensitivity analysis revealed age and gender as important moderators of the effect of obesity on executive and reward functioning, which have implications for intervention or prevention efforts. The performance gap between children with and without obesity was larger for older than younger children on inhibition tasks and marginally so, for attention tasks. Developmental models have identified adolescence as a vulnerable
period for reward-related decision making due to the development of reward functioning outpacing the maturation of executive function (Casey, Jones, & Hare, 2008). Such a model predicts that adolescents ought to show a greater adverse effect of obesity on reward-related decision making, which requires the interaction of executive and reward functioning. Contrary to this prediction, the effect of obesity on reward-related decision making was not significantly moderated by sample age. Perhaps the dissociable effects of sample age on executive and reward-related function relate to differences in the sensitivity of measures or lack of controls for cognitive load or difficulty. They may also reflect a true dissociation in the effect of obesity on executive and reward processes, a ripe area for examination with experimental studies in the future. Nevertheless, it is notable that prevalence of severe obesity (BMI 120% above the 95th percentile) increases from 1.7% in young children to 4.3% in older children and 9% in adolescence (Ogden et al., 2016). Severe obesity is associated with increased likelihood of experiencing multiple medical complications (A. Kelly et al., 2013) and decreased quality of life relative to overweight and obese peers (Zeller et al., 2015). Disproportionately more severely obese children in adolescent samples may intensify the negative effect of adiposity and, therefore, adolescence should be more closely examined for identification of cognitive dysfunction and possible intervention efforts.

Gender moderated effects of obesity such that inhibitory deficits were larger in samples with a greater percentage of females. Although rates of pediatric obesity do not differ by gender (Ogden et al., 2016), worse quality of life due to health comorbidities and depression are seen at higher rates in females than males with obesity (Tsiros et al., 2009; Yagnik, McCormick, Ahmad, & Schecter, 2014). These differences may result in
worse response inhibition for girls with obesity as depression can lead to worse executive functioning (Rock, Roiser, Riedel, & Blackwell, 2014), however, one would also expect that higher rates of depression in females would also negatively affect reward functioning. In adults and adolescents, neural engagement during response inhibition has been seen to differ by gender with greater engagement of frontal-striatal regions in females and greater activation in parietal and motor regions in males (Rubia et al., 2013). Thus, it is possible that those brain-based gender differences underlie the observed moderation of the effect of obesity on response inhibition by gender. Thus, females should be targeted for early intervention and prevention efforts.

Caution in interpretation of the present findings is warranted in light of two observations: First, there are sources of heterogeneity that cannot be controlled. Although statistically significant, some models were not robust against potential unpublished or unknown findings (e.g., Working Memory) and prediction intervals indicated substantial heterogeneity in the distribution of true effects ranging from moderate-large negative effects of obesity to small positive effects (e.g., Interference, Reward-Related Decision Making, and Working Memory). Further, cognitive load or task difficulty is an important source of heterogeneity for executive function. For example, cognitive load differs by the proportion of congruent to incongruent trials on Interference tasks and by the requirement to dynamically update what is maintained in working memory (see Alarcon, Ray, & Nagel, 2016; Pearce, Mackey, Nadler, & Vaidya, Under Review; Zamzow et al., 2014). Such features of study design could not be controlled for because they were either not reported or manipulated in few studies.

Second, socio-demographic and study and task design moderators failed to
explain heterogeneity for most component processes (except inhibition and attention), which may be due to measurement limitations. Greater adiposity was associated with lower IQ and SES, which is consistent with previous reviews (Shrewsbury & Wardle, 2008), however, they did not moderate effects of obesity on executive and reward functioning. The large prediction intervals for these variables indicate substantial heterogeneity in the size of the true effect. Although assessment of IQ is standardized, the construct of SES is not and was assessed differently across studies, potentially contributing to the observed heterogeneity. Only a relatively small proportion of studies reported IQ or SES data, which also may have resulted in reduced power to identify moderation. Further, the failure of included moderators to explain variability across studies highlights a need to include more fine-grained measurement of demographic variables in future studies so that possible correlates of both obesity and executive functioning can be identified.

In sum, the present results provide a comprehensive view of the status of executive and reward-related functioning in pediatric obesity which should motivate future experimental work. Initial evidence suggests that obesity is associated with both structural and functional neural differences in the prefrontal cortex necessary for the control processes examined here (Diamond, 2013) and in fronto-striatal regions, which subserve reward related decision making (Horstmann, 2017). In adolescents, prefrontal engagement during inhibition in the context of food images varied with BMI (Batterink, Yokum, & Stice, 2010). Orbitofrontal cortex, which is sensitive to viewing food versus non-food images (van Meer, van der Laan, Adan, Viergever, & Smeets, 2015) showed greater cortical thinning in adolescents with obesity (Yau et al., 2014) and decreased
white matter connectivity with striatal regions in adults with obesity (Marqués-Iturria et al., 2015). Functional neuroimaging studies targeting the executive and reward-related processes implicated by our findings are needed to formulate mechanistic hypothesis about the role of structural and functional neural dysfunction in obesity. Additionally, our findings identified potential moderators of the effects of obesity that should be further examined in prospective studies, in order to guide targeted avenues for intervention and prevention.
CHAPTER III: SLEEP HEALTH AND PSYCHOPATHOLOGY MEDIATE EXECUTIVE DEFICITS IN PEDIATRIC OBESITY

This chapter has been modified slightly from a submitted article: Pearce, A. L., Mackey, E., Nadler, E. P., & Vaidya, C. J. (Under Review). Sleep Health and Psychopathology Mediate Executive Deficits in Pediatric Obesity.

The role of cognitive processes such as self-regulation (termed executive function) and reward-related motivation in promoting and maintaining obesity is increasingly gaining recognition (Raman et al., 2013). Obesity, observed in 20% of adolescents in the United States (Ogden et al., 2016), is associated with risk for medical co-morbidities (e.g., cardiovascular disease, diabetes; Halfon et al., 2013; Pulgarón, 2013) as well as less academic achievement (Kamijo et al., 2012), and psychosocial problems (e.g., discrimination, self-esteem; Pulgarón, 2013). Models of obesity posit that processes of executive function (i.e., inhibition and working memory) and motivation (i.e., reward sensitivity) are directly pertinent to food intake and non-homeostatic eating (Berthoud et al., 2017; Dohle et al., 2017; Hargrave et al., 2016). Indeed, children with obesity showed greater sensitivity to food rewards (Bonato & Boland, 1983; Sigal & Adler, 1976) and reduced ability to inhibit prepotent responses to food stimuli (Batterink et al., 2010; Nederkoorn, Coelho, Guerrieri, Houben, & Jansen, 2012) and food intake (Maayan, Hoogendoorn, Sweat, & Convit, 2011; Riggs et al., 2010) relative to healthy weight children. However, differences may not be limited to food stimuli, as children with obesity showed higher sensitivity to reward (Fields, Sabet, & Reynolds, 2013; Nederkoorn, Braet, Van Eijs, Tanghe, & Jansen, 2006) and deficits in inhibitory control...
(Maayan et al., 2011; Nederkoorn et al., 2006) and working memory (Groppe & Elsner, 2014; Maayan et al., 2011) without food involvement. Such baseline cognitive impairments are concerning because of their impact on academic outcomes as well as their role in promoting obesogenic behavior.

In formulating a model about cognitive factors in obesity, it is important to note that executive and reward-related functioning are negatively impacted by psychopathology and poor sleep quality, common comorbidities of obesity. Inadequate sleep and poor sleep quality in children are associated with worse academic performance and executive function (Astill, Van der Heijden, van IJzendoorn, & Van Someren, 2012; Beebe, 2011) with sleep disordered breathing, which is common in children with obesity, predictive of behavioral regulation problems longitudinally (Bonuck, Freeman, Chervin, & Xu, 2012). Independent of sleep quality, psychopathology has also been associated with executive dysfunction (Snyder, Miyake, & Hankin, 2015). Furthermore, the two comorbidities have a bidirectional association in adolescents (Alfano, Zakem, Costa, Taylor, & Weems, 2009) and adults such that at 1-year follow up, baseline anxiety and depression predicted new cases of insomnia and baseline insomnia predicted new episodes of anxiety and depression in adults (Jansson-Fröjmark & Lindblom, 2008). While the causal pathways in the relationship between sleep, psychopathology, and cognition remain to be elucidated, sleep quality and psychopathology likely modulate decision-making and executive difficulties observed in pediatric obesity.

The present study examined non-food related reward-related decision-making and executive functioning in children with obesity and the contribution of sleep health and psychopathology. Reward-related decision-making was analyzed for both decision
outcomes and underlying process parameters using Bayesian modeling (Wallsten, Pleskac, & Lejuez, 2005) while executive functioning was examined with tasks requiring reactive response inhibition requiring cancellation of an action after it is planned (Stop Signal Task – SST; Verbruggen & Logan, 2009), dynamic working memory requiring trial-to-trial updating with load manipulation (Jaeggi, Buschkuehl, Perrig, & Meier, 2010), and with ecologically relevant assessment of regulatory and metacognitive executive difficulties using the Behavioral Rating Inventory of Executive Function (BRIEF; Gioia, Isquith, Guy, & Kenworthy, 2000). Sleep quality, assessed by parent report of sleep health using the Children’s Sleep Habits Questionnaire (CSHQ; Owens, Spirito, & McGuinn, 2000), and psychopathology, assessed by parent report of symptoms of DSM-based psychiatric disorders using the Child and Adolescent Symptom Inventory (CASI; Gadow & Sprafkin, 2005), were tested as potential mediators of deficits associated with obesity. Together, this study provides a comprehensive and nuanced examination of decision-making and executive functioning in pediatric obesity with emphasis on contributions of sleep and mental health.

Methods

Participants

Participants included 112 7-18 year old children, of which 105 provided parent-reports of executive functioning and psychopathology, 78 performed the decision-making task, and 59 performed the response inhibition and working memory tasks, with partial overlap across the three samples (Table III-1). Children with obesity (body mass index (BMI) ≥ 95th percentile) was recruited from Children’s National Health System (CNHS) and children without obesity were recruited from the same area communities. Informed
consent and assent was acquired according to guidelines of the Institutional Review Boards of Georgetown University and CNHS.

Full-scale IQ (Wechsler & Hsiao-pin, 2011) was lower in children with obesity across all samples while parental education, age, and gender differed between groups in at least one sample (Table III-1). Exclusion criteria included a current medical diagnosis including insulin resistance or diabetes, psychiatric diagnosis and/or prescription of psychotropic medication, and current or past history of neurological disorders.

**Measures and Procedure**

See supplementary materials for task details (Appendix B).

**Reward-related Decision-Making.** The Balloon Analog Risk Taking Task (BART; Lejuez et al., 2002) had 30 balloon trials. Participants were instructed to pump up balloons without popping them, winning 10 points for each successful pump but losing all points following popping. Participants could save points and get the next balloon at any time. Unbeknown to participants, points saved were exchanged for $5 to ensure ethical treatment of participants.

**Response Inhibition.** A visual SST (Verbruggen, Logan, & Stevens, 2008) presented a fish (go stimulus) facing either left or right, to which participant responded with a button marked “L” or “R”, respectively. Participants were instructed not to respond if the white net appeared (stop signal), which was presented at a variable delay on 1/3 of the trials. The stop signal delay increased or decreased after each successful or unsuccessful stop, respectively, in order to maintain ~0.5 probability of successful inhibition.
Working Memory. Participants completed a letter $N$-back task with consonants only in two runs, 1-back and 2-back, in counterbalanced order. Participants were instructed to respond to serially presented consonants when the letter presented was the same as the letter presented $N$ trials previously (1-back: ‘R’-‘L’-‘L’; 2-back: ‘M’-‘K’-‘M’), with a greater working memory demand for 2-back than 1-back.

Parent-report Questionnaires. A parent completed the BRIEF (Gioia et al., 2000), CSHQ (Owens et al., 2000), and the CASI (Gadow & Sprafkin, 2005). The BRIEF provides T-scores (normed for age and gender; M=50, SD=10) for two indices:
Behavioral Regulation Index (BRI) and Metacognitive Index (MI). The CSHQ characterizes behaviorally based sleep problems and provides estimates of hours slept per night and a Total Score, which encompasses bedtime habits, ability fall and stay asleep, and daytime sleepiness. Average CASI T-scores (normed for age and gender; M=50, SD=10) were calculated for Externalizing (Attention Deficit Hyperactivity Disorder, Conduct Disorder, Oppositional Defiance Disorder) and Internalizing (Generalized Anxiety Disorder, Separation Anxiety, Major Depressive Episode, and Dysthymic Disorder) symptoms, which were categorized as Low Risk (T<60) or At Risk/Clinically Significant (T≥ 60).

**Statistical Approach.** Parental education was controlled for in all analyses with age and gender controlled for in task performance outcomes as BRIEF or CASI indices are already normed for age and gender. Since intellectual functioning may contribute to variability in executive performance, IQ was controlled for in task performance outcomes. Three types of models examined the effect of obesity status (obese vs. non-obese: 1) Analyses of Covariance (ANCOVAs) for all task performance outcomes; 2) Log-linked gamma generalized linear regression for non-parametric BART decision-making parameters; and 3) Logistic regressions for CASI composites indices. Mediation analyses were modeled using adjusted bootstrapping percentile (Rosseel, 2012).

**Results**

**Reward-Related Decision-Making**

Groups did not differ on average number of pumps for balloons that did not pop (F(1, 66)=1.42, p = 0.24, $\eta_p^2= 0.02$) or the number of balloons popped (F(1, 66)=2.33, $p = 0.13, \eta_p^2 = 0.03$; Table III-2). As done in previous studies (Bishara et al., 2009; Rolison,
Hanoch, & Wood, 2012), a Bayesian learning model was used to assess decision-making (Wallsten et al., 2005), with 92% of participants (36 obese, 36 non-obese) showing better fit, estimated via Bayesian Information Criterion, for the Bayesian model than a model assuming no learning (binomial test \( p < 0.01 \)). There were no differences by obesity status for reward sensitivity (\( \gamma \) parameter; \( \beta (se)=0.16 (0.15), e^\beta = 1.17, t = -1.00, p = 0.31 \)). However, response consistency (\( \beta \) parameter), which indexes the extent which participants’ behavior is consistent with their evaluations of risk, differed by obesity status (\( \beta (se)=-0.54 (0.25), e^\beta =0.58 t = -2.16, p = 0.04 \)) such that the ratio of predicted response consistency for children with than without obesity was 0.58. This indicates children with obesity were less able to update and adapt behavior to changing reward contingencies, but did not differ from children without obesity on reward sensitivity or decision-making outcomes.

**Executive Functioning**

**Response Inhibition.** Stop-signal reaction time (SSRT), an estimate of the speed of the inhibitory process, and the stop-signal delay (SSD), the delay length for which a participant successfully inhibited responses 50% of the time, did not differ between groups (SSRT: \( F(1, 53)=0.64, p = 0.43, \eta_p^2= 0.01 \); SSD: \( F(1, 53)=0.21, p = 0.65, \eta_p^2<0.01 \); Table III-2), indicating that inhibitory control of prepotent responses was not affected by obesity.

**Working Memory.** Group X Load (1-back vs. 2-back) ANOVAs were conducted for accuracy (mean percent correct target and non-target responses) and reaction time (RT; Table III-2). For accuracy, a significant effect of Load (\( F(1, 56)=78.2, p < 0.01, \eta_p^2= 0.45 \)) showed worse accuracy for the higher (2-Back: M=84%, SD=13%) than lower
(1-Back: M=97%, SD=5%) load. There was no main effect of Group (F(1, 56) =1.80, p = 0.19, η_p^2= 0.02), however, the interaction (F(1, 56)=4.0, p = .05; η_p^2=0.04) indicated lower accuracy in the obese than non-obese group for the high but not low load (Table III-2).

Reaction times showed a main effect of Load (F(1, 56)=12.8, p < 0.01; η_p^2= 0.13) with slower responses in the higher (2-back: M=709ms, SD=142ms) than lower (1-back: M=641ms, SD=141ms) load, but did not show a main effect of Group (F(1, 52)=1.74, p = 0.10, η_p^2= 0.02) or interaction (F(1, 56)=0.39, p = 0.53, η_p^2<0.01, Table III-2). Together, these results indicate that working memory accuracy but not speed was sensitive to obesity, particularly under more demanding conditions.

<table>
<thead>
<tr>
<th>Table III-2. Task Performance.</th>
<th>Obese</th>
<th>Non-Obese</th>
<th>Difference (95% CI)</th>
<th>d</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stop-Signal Task, ms</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSRT</td>
<td>246 (118)</td>
<td>207 (90)</td>
<td>39 (-15, 94) 0.38</td>
<td>0.15</td>
<td></td>
</tr>
<tr>
<td>SSD</td>
<td>532 (178)</td>
<td>594 (227)</td>
<td>-62 (-169, 44) 0.31</td>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td><strong>N-Back Accuracy, %</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-Back</td>
<td>96 (6)</td>
<td>98 (13)</td>
<td>-2 (-5, 1) 0.42</td>
<td>0.82</td>
<td></td>
</tr>
<tr>
<td>2-Back</td>
<td>80 (4)</td>
<td>88 (11)</td>
<td>-8 (-15, -2) 0.66</td>
<td>0.007**</td>
<td></td>
</tr>
<tr>
<td><strong>N-Back RT, ms</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-Back</td>
<td>664 (126)</td>
<td>599 (150)</td>
<td>65 (-8, 139) 0.22</td>
<td>0.30</td>
<td></td>
</tr>
<tr>
<td>2-Back</td>
<td>722 (137)</td>
<td>682 (148)</td>
<td>40 (-35, 116) 0.22</td>
<td>0.70</td>
<td></td>
</tr>
<tr>
<td><strong>Balloon Analog Risk Taking Task</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted Pumps</td>
<td>30.0 (15.6)</td>
<td>27.6 (12.3)</td>
<td>2.4 (-3.9, 8.7) 0.17</td>
<td>0.45</td>
<td></td>
</tr>
<tr>
<td>Balloons Popped</td>
<td>7.9 (4.2)</td>
<td>6.8 (3.6)</td>
<td>0.9 (-0.6, 2.9) 0.30</td>
<td>0.19</td>
<td></td>
</tr>
<tr>
<td><strong>Behavioral Rating Inventory of Executive Functioning</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Behavior Regulation Index</td>
<td>52.00 (12.28)</td>
<td>46.47 (9.77)</td>
<td>5.53 (0.76, 10.30) 0.52</td>
<td>0.024*</td>
<td></td>
</tr>
<tr>
<td>Metacognition Index</td>
<td>53.31 (11.25)</td>
<td>47.99 (9.76)</td>
<td>5.33 (0.86, 9.79) 0.52</td>
<td>0.020*</td>
<td></td>
</tr>
<tr>
<td><strong>Balloon Analog Risk Taking Task: Decision Making Model</strong></td>
<td>Median (IQR)</td>
<td>Median (IQR)</td>
<td>Difference (95% CI)</td>
<td>d</td>
<td>p</td>
</tr>
<tr>
<td>Response Sensitivity</td>
<td>0.11 (0.13)</td>
<td>0.16 (0.21)</td>
<td>-0.04 (-0.10, 0.00) 0.46</td>
<td>0.04*</td>
<td></td>
</tr>
<tr>
<td>Reward Sensitivity</td>
<td>0.61 (0.83)</td>
<td>0.56 (0.70)</td>
<td>0.09 (-0.09, 0.28) 0.10</td>
<td>0.30</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as mean (SD) and p-values reflect significance of 2-sample t-tests unless otherwise noted. N-Back P values use Tukey adjustment for multiple comparison. SSRT: Stop-signal reaction time; SSD: Stop-signal delay

*a Mann-Whitney-Wilcoxon tests were used for all parameter estimates
*b Mann-Whitney-Wilcoxon's difference in location
*c Cohen's d for medians using pooled median absolute deviation
**Parent Report Questionnaires**

**Executive Function.** Children with obesity had higher scores on both BRIEF indices (BRI: $F(1, 100)=3.85, p=0.05, \eta^2=0.04$; MI: $F(1, 100)=4.32, p=0.04, \eta^2=0.04$), indicating worse parent-reported everyday executive functioning relative to children without obesity.

**Sleep Health.** Despite no difference between groups for hours slept, obesity was associated with higher CSHQ scores ($\beta (se) = 7.64 (2.07), t = 3.69, p<0.01$), indicating sleep health was worse in children with obesity relative to those without obesity (Table III-1).

**Psychopathology.** Obesity status was not related to risk for Externalizing symptomology ($\beta (se) = 0.66 (0.70), z = 0.95, p = 0.34$). However, children with obesity experienced 4.27 greater odds of scoring above the At Risk/Clinically Significant cutoff for Internalizing symptoms relative to children without obesity ($\beta (se) = 1.45 (0.64), z = 2.30, p = 0.02$).

**Mediation Analyses**

Neither CSHQ nor internalizing symptomology were associated with performance during 2-Back (CSHQ: $\beta (SE) = -0.002 (0.001), t = -1.05, p = 0.29$; Internalizing: $\beta (SE) = 0.02 (0.05), t = -0.37, p = 0.72$) or response consistency (CSHQ: $\beta (se) = -0.01 (0.02), e^\beta = -0.79, t = -0.79, p = 0.44$; Internalizing: $\beta (se) = -0.45 (0.49), e^\beta = 1.17, t = -0.93, p = 0.36$). Therefore, 2-Back performance and response consistency were not tested for the mediation by sleep or psychopathology. In contrast, both CSHQ scores and internalizing symptoms were associated with BRI (CSHQ: $\beta (SE) = 0.44 (0.15), t = 2.91, p <0.01$;
Internalizing: $\beta$ (SE) = 14.6 (3.92), $t = 3.73$, $p < 0.01$ and MI (CSHQ: $\beta$ (SE) = 0.47 (0.15), $t = 3.06$, $p < 0.01$; Internalizing: $\beta$ (SE) = 12.27 (3.98), $t = 3.09$, $p < 0.01$) scores, indicating that children with worse sleep health or with At Risk/Clinically Significant levels of Internalizing symptoms were more likely to show worse parent-reported everyday executive functioning.

Separate multiple mediation models, including age, gender, and parental education as covariates, were conducted for BRI and MI scores (Figures III-1A and III-1B). The covariance between CSHQ total score and Internalizing symptom category was equivalent for both mediation models (cov (se)= 0.61 (0.30), $z = -2.04$, $p = 0.04$. Despite significant covariance, both mediators showed significant indirect effects for BRI (CSHQ: $\beta$ (SE) = 3.05 (1.41), $z = 2.16$, $p = 0.03$; Internalizing: $\beta$ (SE) = 3.46 (3.46), $z =$
2.38, \( p = 0.02 \) and MI (CSHQ: \( \beta \) (SE) = 3.20 (1.44), \( z = 2.22, p = 0.03 \); Internalizing: \( \beta \) (SE) = 2.84 (1.32), \( z = 2.15, p = 0.03 \). There were no differences in the strength of the indirect effects of the two mediators (BRI: \( \beta \) (SE) = -0.42 (2.06), \( z = -0.20, p = 0.84 \); MI: \( \beta \) (SE) = 0.36 (2.01), \( z = 0.18, p = 0.86 \). The direct effects between obesity status and worse scores on BRIEF indices became non-significant after inclusion of the mediators (Figure III-2A and B), thus, the presence of poorer sleep health and At Risk/Clinically Significant levels of Internalizing symptoms mediated effects of obesity status on executive functioning as measured by parent report of everyday behavior.

**Discussion**

Pediatric obesity was associated with impairment in select components of reward related decision-making and executive functioning with poorer sleep health and greater risk of internalizing psychopathology mediating everyday executive behavioral deficits. Children with obesity did not differ for reward related decision-making outcomes or sensitivity to monetary reward, but showed reduced ability to adapt behavior to changing reward contingencies. While inhibitory performance did not differ, children with obesity showed executive dysfunction under higher working memory demands and in everyday behavioral regulation and metacognition. Parent reports indicated that children with obesity had poorer sleep quality, despite equal sleep durations, and four times greater risk for experiencing internalizing psychopathology. Importantly, sleep health and internalizing symptoms mediated the deleterious effect of obesity on everyday behavioral regulation and metacognitive abilities but not on decision-making and working memory performance. Our results highlight significant vulnerabilities for cognitive, sleep, and
mental health of children with obesity, while elucidating a potential path through which obesity impacts everyday executive behaviors.

Children with obesity’s decision-making performance was atypical in ways that could have significant impact upon the maintenance of their obesity status. The Bayesian decision-making model for the BART (Wallsten et al., 2005) had never previously been applied in studies of obesity and showed that despite lack of group differences in reward-related behavioral outcomes (i.e., number of pumps and pops), children with obesity showed responses that tended to be less sensitive to estimation of risk, suggesting decision-making that was less informed by one’s own evaluation of risk/reward across trials. Such nuanced examination of decision-making may explain why tasks similar to the BART (e.g. Door Opening task, Hungry Donkey Task) have mixed findings with some showing greater reward sensitivity in pediatric obesity (Nederkoorn et al., 2006; Verbeken, Braet, Bosmans, & Goossens, 2014; Verdejo-García et al., 2010) while others have not (Groppe & Elsner, 2014; Guerrieri, Nederkoorn, & Jansen, 2007; Scholten, Schrijvers, Nederkoorn, Kremers, & Rodenburg, 2014), as a tendency to make decisions that are inconsistent with own reward/risk evaluation may not be consistently captured in observable outcomes. Identifying specific reward-related biases in obesity is important for guiding prevention/intervention efforts.

Performance-based and ecologically relevant examination of executive function revealed impairments that may negatively impact academic achievement and social interaction. Unlike past findings using auditory stop signals (Kulendran et al., 2014; Nederkoorn et al., 2006) we did not observe group differences using visual stop signals. It is possible that inhibitory control is more challenging under cross-modal conditions.
(i.e., auditory stop signal and visual go cue), suggesting that response inhibition deficits may only be seen under more challenging demands. Indeed, impairment in dynamic working memory in children with obesity was limited to the higher load condition in the present study. Past studies show mixed findings using span tasks, which require active maintenance without dynamic updating (Cserjési, Molnár, Luminet, & Lénárd, 2007; Groppe & Elsner, 2014; Maayan et al., 2011). Dynamic working memory correlates with academic performance and is highly predictive of overall intellectual function (Jaeggi, Buschkuehl, Jonides, & Perrig, 2008); we controlled for IQ, thus, the observed deficit was above and beyond that accounted for by general intelligence. Assessment of everyday behavior with the BRIEF revealed that children with obesity were more likely to exhibit impairment on the Behavioral Regulation factor (i.e., inhibitory, emotion regulation, and set switching) and the Metacognition factor (i.e., working memory, planning, organization, and monitoring abilities; Gioia, Isquith, Retzlaff, & Espy, 2002). Working memory, behavioral regulation, and metacognitive executive deficits are likely to interfere with academic achievement as well as social interaction (Alduncin, Huffman, Feldman, & Loe, 2014).

Parent reported sleep health and psychopathology accounted for significant variance in the observed effects of obesity on executive functioning. Worse sleep quality and greater odds of clinically relevant internalizing symptomatology in children with obesity, as observed in this study, are consistent with previous studies (Beebe et al., 2007; Panossian & Veasey, 2012; Pulgarón, 2013; Yagnik et al., 2014). Both factors, however, are associated with executive functioning, independent of obesity. Association with sleep (Beebe, 2011) may stem from repeated deprivation of oxygen during sleep apnea and/or
from attention problems induced by daytime sleepiness. Internalizing symptoms are defined as over-regulated behavior and are highly comorbid with disorders of executive function such as Attention deficit hyperactivity disorder (Snyder et al., 2015). Here, both sleep health and internalizing symptomology significantly mediated the effect of obesity on executive functioning expressed in everyday behaviors but not in performance. The chronic effects of poor sleep and internalizing symptomology may be more readily apparent in spontaneous behavior over time rather than in a laboratory setting where children can muster the motivation to overcome attention problems for the short duration of the task. Further experimental work including intervention designs are needed to disambiguate the causal relations between obesity, sleep health, internalizing psychopathology, and executive function.

Interpretation of the results is constrained by three challenges that are not specific to the present study. First, the effect of obesity is confounded by lower SES and intellectual functioning, both of which covary with lower executive function and worse psychological wellbeing, independent of obesity status. We controlled for these statistically with well accepted proxy measures, namely parental education for SES and full scale IQ for intellectual function. Parental education was chosen as it has been more consistently associated with pediatric obesity than family income levels (Shrewsbury & Wardle, 2008). Second, whether our results relate to causes or consequences of obesity cannot be discerned by the present study design. Children were not undergoing treatment for diabetes, however, presence of undiagnosed cases cannot be ruled out. Physiological factors associated with obesity such as brain inflammation due to increased free-fatty acids (A. A. Miller & Spencer, 2014) and insulin dysregulation (Zhang et al., 2009) could
negatively impact neuronal functioning in frontal lobe regions (A. A. Miller & Spencer, 2014), which are important for decision-making and executive function and promote the development of depression (Soczynska et al., 2011). Study designs that manipulate inflammatory/metabolic functioning (i.e., comparison before and after weight loss) are necessary to disambiguate cause versus consequence of obesity on cognitive and psychological function. Lastly, psychopathology was measured with parent report, which is thought to be more valid in younger children than in adolescents particularly for internalizing symptoms. Self-report measures would be important to include in future work.

Results underscore the importance of early intervention and prevention, as cognitive deficits likely worsen as cognitive and social adaptive demands increase with age. Worse reward-related decision-making and risk for internalizing disorders are particularly important during adolescence, when social influence on risk-taking behavior and risk for developing psychopathology is highest (Paus, Keshavan, & Giedd, 2008). Additionally, depressive symptoms have been shown to contribute to persistence of obesity in adolescence (Goodman & Whitaker, 2002), highlighting the importance of understanding the causal relationships between internalizing symptoms, obesity, and executive functioning. While our findings should be replicated with objective assessment of sleep health, they suggest at least some aspects of executive dysfunction in obesity could be alleviated by improving sleep health and psychopathology.
CHAPTER IV: ALTERED NEURAL BASES OF MEMORY, EXECUTIVE FUNCTION, AND REWARD IN ADOLESCENT OBESITY

This chapter has been modified slightly from an article that is being prepared for submission: Pearce, A. L., Cherry, JBC., You, X., Olson, A., Mackey, E., Nadler, E. P., & Vaidya, C. J., (in prep). Altered Neural Bases of Memory, Reward, and Executive Function in Pediatric Obesity.

In the United States, 20% of adolescents meet criteria for obesity (body mass index—BMI—above the 95th percentile), however, a growing number have very high BMIs with 8% and 2% of adolescents meeting criteria for severe (BMI 120% above the 95th percentile; Ogden et al., 2016) or morbid obesity (140% of the 95th percentile; Skinner & Skelton, 2014), respectively. Adolescents with severe obesity are more likely to experience multiple medical complications with high morbidity (A. Kelly et al., 2013) and to report worse quality of life relative to adolescents with overweight and obesity (Zeller et al., 2015). Along with serious medical consequences, pediatric obesity has been associated with increased risk for externalizing (e.g., attention-deficit hyperactivity disorder) and internalizing psychopathology (e.g., anxiety, depression; Halfon et al., 2013; Pulgarón, 2013), psycho-social difficulties (e.g., discrimination and self-esteem; Pulgarón, 2013), worse academic achievement (Kamijo et al., 2012), and neurocognitive deficits related to executive (i.e., working memory, inhibitory control, and cognitive flexibility) and reward function (Reinert et al., 2013; Thamotharan et al., 2013). Neurocognitive deficits, in particular, represent a target for intervention as they
contribute to the development and maintenance of pediatric obesity by increasing risk for obesogenic behaviors (Berthoud et al., 2017; Dohle et al., 2017; Hargrave et al., 2016).

Executive, reward, and mnemonic processing interact to enable reward related decision making that either leads to engagement in or avoidance of obesogenic behaviors. Worse executive and reward function in children has been associated with increased likelihood to consume energy dense foods and beverages (De Decker et al., 2016; Riggs et al., 2010), while worse episodic memory in adults was predictive of more unconstrained and emotional eating (Martin et al., 2017). In contrast, better executive abilities in children were associated with less snack food intake (Riggs et al., 2010) and a greater likelihood of maintaining a healthy body weight into adolescence (Duckworth et al., 2010), while better episodic memory in adults was associated with avoidance of fatty foods (Martin et al., 2017). Self-regulatory abilities in children have also been shown to mediated the association between food sensitivity and snacking behaviors (Stok et al., 2015). Similarly, food and meal related memories may influence reward-related decision making through the inhibition appetitive cues with deficits in episodic memory resulting in more automatic or habitual responses to food rewards (Higgs, 2016). Thus, although executive, reward, and mnemonic processes have independent associations with obesogenic behaviors, executive and mnemonic processes may help regulated reward-related motivations (Dohle et al., 2017; Higgs, 2016).

Obesity is associated with altered neural responses to food stimuli in regions subserving executive, reward, and mnemonic function. Across adults and children, obesity was associated with greater activation to food stimuli in regions subserving reward (e.g. dorsomedial prefrontal cortex) and mnemonic (e.g., parahippocampal gyrus)
function (Brooks, Cedernaes, & Schiöth, 2013), which may suggest a disproportionate reward response to food stimuli (Stice & Yokum, 2016). Indeed, adolescents who showed greater activation of reward related regions in response to food commercials had greater BMI gains one year later (Yokum, Gearhardt, Harris, Brownell, & Stice, 2014). Thus, increased responsiveness of reward related neural circuitry may serve to increase risk for obesogenic behaviors. In contrast, adults and children with obesity showed reduced activation to food stimuli in regions subserving executive function (e.g., dorsolateral prefrontal cortex; Brooks et al., 2013), which may suggest a deficient inhibitory response to food stimuli (Stice & Yokum, 2016). This interpretation is supported by a study showing that adolescents girls with higher BMIs showed reduced lateral prefrontal activation during an inhibitory task using food stimuli. (Batterink et al., 2010). However, it is unclear if these patterns of aberrant functional neural circuitry associated with obesity are limited to food stimuli or reflect more general neurocognitive deficits.

In order to determine if differential engagement of regions related to executive, reward, and mnemonic function are specific to appetitive cues or represent altered function neural circuitry, the present study will examine neurocognitive function outside the food context. This will be the first study to examine neural function during executive and reward tasks without the use of food-related stimuli in adolescents with obesity and the first to examine neural functioning during encoding of episodic information in individuals with obesity. Executive, reward, and mnemonic processing are all required during reward related decision making such that deficits in any of these processes may result in less adaptive decision making. Thus, decision making modeling will be used to examine reward related process biases associated with obesity. If neurocognitive deficits
and altered function neural circuitry persist beyond the food-context, it would suggest that obesity is associated with domain general deficits that impact both food and non-food related behavioral regulation and decision making.

**Materials and Methods**

**Participants**

Sixty-two adolescents (M=16.8, SD=1.60) who either had severe or morbid obesity without medical comorbidities (SMOB; n = 33) or did not have obesity (HW; BMI < 95th percentile; n=29) were enrolled. Participants with SMOB were recruited from Children’s National Health System (CNHS) in Washington, DC, while participants with HW were recruited from the general Washington, DC metropolitan area. Informed consent and assent was obtained according to the guidelines of the Institutional Review Boards at Georgetown University and CNHS. Participants with a BMI ≥ 50 were unable to be scanned due to size constrains and completed all tasks outside of the scanner. Thus, participants with HW were oversampled with a random subset only completing tasks outside the scanner in order to achieve similar sample sizes for behavioral data. The final imaging subset included 35 participants (SMOB = 18; HW = 17). All participants were required to have a full-scale IQ ≥ 75 (estimated from the vocabulary and matrix reasoning subtests of the Wechsler Abbreviated Intelligence Scale-II; Wechsler & Hsiao-pin, 2011), no past or current diagnosis of Type 2 diabetes or neurological disorder, based on parent reports.

Adolescents with SMOB had higher BMIs than adolescents without obesity (Table IV-1), however, age, gender, ethnicity, and race did not differ across groups. In the imaging subset, groups did not differ on IQ, years of maternal education, or annual
family income, however, in the full sample, adolescents with SMOB had lower IQs and annual family income and fewer years of maternal education than adolescents with HW (Table IV-1).

Table IV-1. Demographic Characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Behavioral Sample</th>
<th>MRI Sample</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Obese</td>
<td>Not Obese</td>
</tr>
<tr>
<td><strong>BMI Baseline</strong></td>
<td>46.12 (7.54)***</td>
<td>21.51 (2.38)***</td>
</tr>
<tr>
<td><strong>Age, yr.</strong></td>
<td>16.84 (1.54)</td>
<td>16.79 (1.54)</td>
</tr>
<tr>
<td><strong>IQ</strong></td>
<td>96.43 (11.52)**</td>
<td>107.50 (12.02)**</td>
</tr>
<tr>
<td><strong>Maternal Ed, yrs.</strong></td>
<td>13.74 (4.23)***</td>
<td>16.34 (2.19)***</td>
</tr>
</tbody>
</table>

| **Sample Sizes, N**  | 24                | 26          | 15              | 15 |
|                      | Episodic Memory   |            |                |    |
|                      | N-Back            | 26          | 27              | 18  |
|                      | MID               | --          | --              | 17  |
|                      | BART              | 31          | 29              | --  |
| **Gender, N**        | Male              | 9           | 10              | 6   |
|                      | Female            | 24          | 19              | 12  |
| **Handedness, N**    | Right             | 29          | 27              | 15  |
|                      | Left              | 4           | 2               | 3   |
| **Ethnicity, N**     | Hispanic/Latino   | 7           | 4               | 4   |
|                      | Not H/L           | 23          | 25              | 13  |
|                      | Not Reported      | 3           | 0               | 1   |
| **Race, N**          | Black/AA          | 17          | 7               | 9   |
|                      | White             | 8           | 17              | 5   |
|                      | Other/Mixed       | 5           | 5               | 4   |
|                      | Not Reported      | 3           | 0               | 0   |
| **SES, N**           | >$80,000          | 10*         | 17*             | 8   |
|                      | $50,000-$80,000   | 6*          | 6*              | 4   |
|                      | <$50,000          | 14*         | 5*              | 6   |
|                      | Not Reported      | 3*          | 0*              | 0   |

Group differences tested with t-tests or Fisher's Exact test; *p<0.05; **p<0.01; ***p<0.005; BART: Balloon Analog Risk Taking Task; MID: Monetary Incentive Delay Task

**Experimental Design and Statistical Analysis**

Participants performed episodic memory encoding, working memory, and reward anticipation tasks during fMRI and recognition memory and reward-related decision making tasks outside the scanner. All tasks were administered using E-Prime.
and were practiced prior to completing the experimental portion. Stimuli for the fMRI tasks were viewed through a mirror mounted on the head coil and presented using a magnet-compatible projector. Tasks completed outside of the scanner were administered using a laptop computer. For both reward-related tasks, participants were informed that the points earned during the tasks would be exchanged for a monetary reward. Unbeknown to the participants, all participants received $5 for each task in order to ensure ethical treatment of all participants.

**Working Memory.** Working memory was assessed via a verbal N-back task. While viewing serially presented consonants (1 s presentation, 3 s inter-stimulus-interval—ISI), participants were instructed to respond with a button press when the current letter matched the letter presented \( N \) times ago. Participants completed three blocks for each load with 1-back (‘K’–‘P’–‘P’), 2-back (‘L’–‘P’–‘K’–‘P’), and 3-back (‘P’–‘L’–‘K’–‘P’) loads occurring in Latin Square order and separated by fixation blocks (14 s). Each block presented the block instruction (i.e., “1-back”, “2-back”, or “3-back”; 4 s) followed by 9 stimuli trials for a total of 81 stimuli (16 targets) and a run time of 7.84 min.

**Reward Anticipation.** Reward anticipation was assessed via the Monetary Incentive Delay Task (MID; Knutson, Adams, Fong, & Hommer, 2001). Each trial of the MID presented a cue (2000 ms), followed by the target (160-360 ms) and trial feedback (1920 ms). Participants were instructed to respond to the target as quickly as possible because if they responded while the target remained on the screen they would win points (gain/circle cue trials) or avoid losing points (loss/square cues), however, if they responded too slowly they would miss gaining points (gain/circle cues) or lose points.
(loss/square cues). Cues signaled either no response (triangles, n = 18), potential for gain (circles = 36), or potential for loss (squares, n = 36), with the number of lines inside the cue shapes indicating the points at stake: no lines—0 pts, 1 line—0.5 pts, 2 lines—1 pt, and 3 lines—5 pts (n = 9 each for gain and loss). The duration of the target was adjusted trial-by-trial (20 ms) to ensure the target hit rate was 66%. Individualized starting target durations were determined from the participant’s average reaction time during practice. Fixations before and after the target were adjusted trial-by-trial to ensure each trial lasted 8 s, resulting in a run time of 12 min.

**Reward Related Decision-Making.** Decision making was assessed via the Balloon Analog Risk Taking task (BART; Lejuez et al., 2002), which was administered out of the scanner. Each trial (n=30) presented a balloon that participants were instructed to pump up as large as they could without popping, winning 10 points for each successful pump and losing all points for that balloon if it popped. Participants could save their points and get the next balloon at any time. Each balloon had a different point of popping and the probability of a balloon popping changed with each pump such that the first pump represented a 1/128 chance of popping, the second a 1/127 chance, and so on until the 128th pump which would result in a 1/1 chance of popping.

**Episodic Memory.** Episodic memory was assessed via a subsequent memory paradigm. While viewing serially presented color images (2 s), participants were instructed to indicate whether they depicted indoor or outdoor scenes. Trial presentation was event-related with jitter optimized for selective averaging using OPTSEQ2 (https://surfer.nmr.mgh.harvard.edu/optseq/), resulting in a scan time of 6.13 min. In order to increase interference and prevent ceiling effects for the recognition of scenes
viewed in the scanner, a distractor task was administered outside the scanner where participants encoded 46 novel scenes (1.5 s, 0.5 s ISI). Following the distractor task, a self-paced surprise recognition memory task serially presented 184 scenes that participants were instructed to identify as “New” (i.e., not previously presented; 92 images) or “Old” (i.e., scene was previously presented; 92 images). The sets of scenes presented during the scan, as distractors, and as retrieval foils were randomly assigned and counterbalanced across participants.

**Image Acquisition Parameters.** Imaging was performed on a 3T Trio Siemens scanner (Erlangen, Germany). A high resolution T1-weighted structural scan (MPRAGE) was acquired lasting 7.23 mins with the parameters: TR/TE=2300/2.94ms, TI=900ms, 90-degree flip angle, 1 slab, 160 sagittal slices with a 1.0 mm thickness, FOV=256x256mm², resulting in an effective resolution of 1.03mm isotropic voxels. Three functional runs were acquired using a T2*-sensitive gradient echo pulse sequence with parameters: TR/TE=2000/30ms, 90-degree flip angle, 43 interleaved slices (width = 2.5mm, gap width = 0.5mm, effective width = 3mm) ascending in the transverse plane, FOV=192x192mm². Slice acquisition was parallel to orbitofrontal cortex for N-back and MID runs to minimize susceptibility artifacts and was angled in the plane of the hippocampus to optimize medial temporal lobe signal during the episodic encoding scan. Head movement was minimized with padding between the head and coil.

Functional images were analyzed using SPM12 (Wellcome Department of Cognitive Neurology, London, UK). Preprocessing included discarding the first 4 TRs for signal stabilization, correction for motion as suggested by Wilke, (2012), slice-time correction, co-registration to each participant’s MPRAGE, and smoothing with an 8mm
FWHM Gaussian kernel. Responses were modeled using a canonical hemodynamic response function which was convolved with trial/block onset vectors specific to each task. For each subject, general linear model models included task-specific contrasts in addition to 7 regressors of no interest: 6 realignment parameters derived to estimate the effect of head motion on signal (Wilke, 2012) and 1 parameter which de-weighted volumes with greater than 1.5 mm motion scan-to-scan (STS). Task contrasts of interest were: 1) N-Back: 2-Back > 1-Back (the 3-back blocks were not included in imaging analyses due to poor accuracy, see Results section); 2) MID: reward > no reward/neutral circle cues (loss cues were not modeled as only reward anticipation was of interest in the current study); and 3) Episodic memory: encoded scenes that were subsequently remembered > forgotten (participants with fewer than 5 scans per condition were excluded from analyses). Participants with more than 10% of volumes with half a voxel (1.5 mm) or greater motion STS were excluded from analyses (see Table IV-1 for final sample included in analyses for each task). Deformation fields derived from participant’s MPRAGE were applied to contrast maps to normalize into MNI standard stereotaxic space.

**Statistical Analyses.** All behavioral analyses were completed in R (R Core Team, 2014) and all group imaging analyses were conducted using GLM Flex Fast2 (http://mrtools.mgh.harvard.edu/). Behavioral analyses assessed group differences using analyses of covariance (ANCOVAs), controlling for maternal education and IQ. Effect sizes were calculated using Cohen’s d (t-tests) and partial eta-squared (ηp2; ANCOVAs). Multiple comparisons were controlled for at $p < 0.05$ using Tukey-corrected pairwise post-hoc tests. Non-parametric parameters obtained from the BART Bayesian decision
making model (details reported in results; see model 3 in Wallsten et al., 2005) were analyzed using gamma generalized linear models with a log link function. Imaging analyses assessed group differences in activation using general linear models controlling for mean motion STS and age. Multiple comparisons were controlled for at \( p < 0.05 \) using whole-brain Monte-Carlo simulations with 3dclustsim (2-sided, nearest neighbor 2; \( k=121, p=0.005 \); Cox, Chen, Glen, Reynolds, & Taylor, 2017).

**Results**

**Working Memory**

For behavioral analyses, Group (obese vs non-obese) x Load (1- vs 2-Back) ANCOVAs were conducted for reaction time (RT) and balanced accuracy \( \left( \frac{\% \text{hits} + (1-\% \text{FA})}{2} \right) \). The covariates were not related to RT (maternal education: \( p = 0.18 \); IQ: \( p = 0.38 \)). RT showed a main effect of Load (\( F(2, 96) = 5.88, p < 0.01, \eta^2_p = 0.09 \)) such that responses were slower during 3-Back (\( M = 692 \text{ ms}, \text{SD} = 268 \text{ ms} \)) than 1-Back (\( M=584 \text{ ms}, \text{SD}=166 \text{ ms}, p_{\text{Corrected}} = 0.03, d = 0.48 \)) and 2-Back (\( M = 579 \text{ ms}, \text{SD} = 206 \text{ ms}, p_{\text{Corrected}} = 0.02, d = 0.47 \)) loads, but did not differ between 1- and 2-Back loads (\( p_{\text{TukeyCorrected}} = 0.994 \)). There was no main effect of Group (\( F(1, 46) = 2.48, p = 0.12, \eta^2_p = 0.02 \)) or a Group x Load interaction (\( F(2, 96) = 1.22, p = 0.30, \eta^2_p = 0.02 \)), indicating overall response speed and the effect of load on response speed did not differ by obesity status.

The covariate maternal education was not related to balanced accuracy (\( p = 0.44 \)), however, IQ was positively associated with accuracy (\( F(1, 46) = 12.25, p < 0.01, \eta^2_p = 0.09 \)) such that those with higher IQs performed better. Through the inclusion of these covariates, the effect of IQ on accuracy was accounted for in all observed effects.
Table IV-2. Performance During Episodic Memory, N-Back, Monetary Incentive Delay, and Balloon Analog Risk Taking Tasks.

<table>
<thead>
<tr>
<th>Task</th>
<th>Performance Measure</th>
<th>Obese Mean (SD)</th>
<th>Not Obese Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Episodic Memory Task</td>
<td>Corrected Accuracy</td>
<td>45.8 (38.8)</td>
<td>49.5 (35.6)</td>
</tr>
<tr>
<td>N-Back</td>
<td>Accuracy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-Back</td>
<td>94.7 (11.5)</td>
<td>97.8 (4.7)</td>
<td></td>
</tr>
<tr>
<td>2-Back</td>
<td>89.5 (13.1)</td>
<td>96.2 (6.6)</td>
<td></td>
</tr>
<tr>
<td>3-Back</td>
<td>78.4 (15.1)</td>
<td>89.8 (11.6)</td>
<td></td>
</tr>
<tr>
<td>Reaction Time, ms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-Back</td>
<td>644 (192)</td>
<td>526 (113)</td>
<td></td>
</tr>
<tr>
<td>2-Back</td>
<td>633 (249)</td>
<td>528 (141)</td>
<td></td>
</tr>
<tr>
<td>3-Back</td>
<td>707 (305)</td>
<td>677 (232)</td>
<td></td>
</tr>
<tr>
<td>Monetary Incentive</td>
<td>Total Points</td>
<td>11.7 (12.2)</td>
<td>12.1 (10.9)</td>
</tr>
<tr>
<td>Delay Task</td>
<td>Reaction Time, ms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutral: 0 points</td>
<td>193.4 (19.8)</td>
<td>173.3 (25.6)</td>
<td></td>
</tr>
<tr>
<td>Low: 0.5 points</td>
<td>193.9 (19.3)</td>
<td>174.9 (29.8)</td>
<td></td>
</tr>
<tr>
<td>Medium: 1 point</td>
<td>195.2 (24.3)</td>
<td>172.8 (31.4)</td>
<td></td>
</tr>
<tr>
<td>High: 5 points</td>
<td>191.6 (19.7)</td>
<td>170.6 (24.2)</td>
<td></td>
</tr>
<tr>
<td>Balloon Analog Risk</td>
<td>Adjusted Number of</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Taking Task</td>
<td>Pumps c</td>
<td>33.4 (14.3)</td>
<td>31.7 (10.9)</td>
</tr>
<tr>
<td>Balloons Popped</td>
<td>8.4 (4.3)</td>
<td>8.8 (2.7)</td>
<td></td>
</tr>
<tr>
<td>Total Points</td>
<td>6,666 (1,822)</td>
<td>6,493 (1,683)</td>
<td></td>
</tr>
</tbody>
</table>

a: Corrected accuracy: % correctly remembered - % False Alarms
b: Accuracy calculated as the average % correct hits and % correct rejections
c: Average number of pumps for balloons that did not pop

Balanced accuracy showed a main effect of Load (F(2, 96) = 26.19, p < 0.01, ηp² = 0.31), such that accuracy was worse during 3-Back (M = 84.2%, SD = 14.5%) than 1-Back (M = 96.3%, SD = 8.7%, p_corrected < 0.01, d = 1.01) and 2-Back (M = 93.0%, SD = 10.8%, p_corrected < 0.01, d = 0.68) loads, but did not differ between 1- and 2-Back loads (p_corrected = 0.28, d = 0.34). The main effect of Group approached significance (F(21, 46) = 3.79, p = 0.06, ηp² = 0.03) such that adolescents with SMOB had worse accuracy than adolescents with HW (Table IV-2). Additionally, there was a significant Group x Load interaction (F(2, 96) = 3.27, p = 0.04, ηp² = 0.05) which showed worse performance for adolescents with SMOB than with HW during 3-Back (p_corrected < 0.01), but no group differences for 1-Back (p_corrected = 0.91) or 2-Back (p_corrected = 0.24) loads (Table IV-2).
This suggests the performance deficit observed in adolescents with SMOB, relative to those with HW, increased as the working memory load increased.

**Figure IV-1. Clusters Showing Greater Activation for Adolescents With than Without Obesity During the N-back Task Indexing Executive Function, Controlling for Mean Motion Scan-to-Scan and Age; p<0.05, corrected.**

For imaging analyses, the 3-Back load was excluded because the number of correct hits was below chance in over 20% of adolescents with SMOB in the full sample (n = 6 of 26) and over 25% in the imaging subset (n = 5 of 18). Adolescents with SMOB showed greater activation for 2-Back than 1-Back loads relative to adolescents with HW in frontal, striatal, temporal, and partial regions (Table IV-3, Figure IV-1). Frontal and striatal clusters included the right superior and medial frontal gyri and the putamen and caudate. There were also bilateral middle temporal clusters with the right hemispheric cluster extending into the right angular and middle occipital gyri and left hemispheric cluster extending into the superior temporal gyrus. Similarly, there were bilateral postcentral clusters with the right hemispheric cluster extending into the precentral gyrus.
and left hemispheric cluster extending into the supramarginal and inferior parietal gyri. Despite no group differences in performance during 1- and 2-back loads, adolescents with SMOB showed greater neural engagement of frontal-parietal regions during working memory, potentially indicating inefficient neural processing or greater effort relative to adolescents with HW.

Table IV-3. Peak Activations from Clusters Showing Greater Activation for Adolescents With than Without Obesity During the N-back Task Indexing Executive Function, Controlling for Mean Motion Scan-to-Scan and Age.

<table>
<thead>
<tr>
<th>Region (BA)</th>
<th>H</th>
<th>Volume</th>
<th>t</th>
<th>x</th>
<th>y</th>
<th>z</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior and Medial Frontal Gyri (9, 10)</td>
<td>R</td>
<td>122</td>
<td>3.38</td>
<td>4</td>
<td>62</td>
<td>28</td>
</tr>
<tr>
<td>Precentral and Postcentral Gyri (6)</td>
<td>R</td>
<td>185</td>
<td>3.76</td>
<td>58</td>
<td>2</td>
<td>28</td>
</tr>
<tr>
<td>Postcentral, Inferior Parietal, and Supramarginal Gyri (2, 40)</td>
<td>L</td>
<td>1338</td>
<td>4.63</td>
<td>-40</td>
<td>-16</td>
<td>38</td>
</tr>
<tr>
<td>Superior and Middle Temporal Gyri (22)</td>
<td>L</td>
<td>221</td>
<td>4.14</td>
<td>-42</td>
<td>-52</td>
<td>12</td>
</tr>
<tr>
<td>Middle Temporal, Angular, and Middle Occipital Gyri (39, 19)</td>
<td>R</td>
<td>1339</td>
<td>4.91</td>
<td>46</td>
<td>-78</td>
<td>34</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4.47</td>
<td>46</td>
<td>-84</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4.32</td>
<td>48</td>
<td>-58</td>
<td>8</td>
</tr>
<tr>
<td>Putamen and Caudate into Rectus</td>
<td>R</td>
<td>330</td>
<td>4.32</td>
<td>10</td>
<td>8</td>
<td>-14</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3.1</td>
<td>18</td>
<td>4</td>
<td>-10</td>
</tr>
</tbody>
</table>

a: volume measured in mm$^3$; b: peak t-value derived from the general linear model
BA: Broadmann's Area; H: hemisphere

**Reward Anticipation**

For behavioral analyses, a Group x Reward Value (neutral vs. low vs. medium vs. high) ANCOVA was conducted for RT and a one-way ANCOVA was conducted for total points. The covariates were not related to response speed (maternal education: p = 0.22; IQ: p = 0.71) or points earned (maternal education: p = 0.85; IQ: p = 0.12). RT did not show a main effect of Reward Value ($F(1, 29) = 0.54, p = 0.66, \eta_p^2 = 0.02$), indicating that speed did not differ across levels of reward. There was, however, a main effect of Group ($F(1, 29) = 4.50, p = 0.04, \eta_p^2 = 0.05$) such that adolescents with SMOB had slower responses than adolescents with HW (Table IV-2). The Group x Reward Value...
interaction was not significant (F(1, 29) = 0.08, p = 0.97, $\eta^2_p < 0.01$), indicating that the effect of Group did not differ across levels of reward. Total points earned did not differ by Group (F(1, 29) = 0.03, p = 0.87, $\eta^2_p < 0.01$; Table IV-2).

For imaging analyses, a Group x Anticipated Reward Value (low > no reward vs medium > no reward vs high > no reward) ANCOVA was conducted. The main effect of reward value showed greater activation for higher than lower levels of reward across frontal, striatal, and parietal regions related to reward processing (Table IV-4). The largest cluster included bilateral superior and middle frontal gyri, extending into bilateral pre/postcentral gyri, supplementary motor area, anterior and middle cingulate cortex, insula, caudate, and thalamus. Additionally, there were clusters in left middle frontal

Figure IV-2. Anticipation of Reward for the Showing Monetary Incentive Delay Task, Controlling for Mean Motion Scan-to-Scan and Age; p<0.05, corrected. A) Clusters Showing Greater Activation for Adolescents Without than With Obesity; B) Group x Reward Value Interaction; *p<0.05, Tukey Corrected.

For imaging analyses, a Group x Anticipated Reward Value (low > no reward vs medium > no reward vs high > no reward) ANCOVA was conducted. The main effect of reward value showed greater activation for higher than lower levels of reward across frontal, striatal, and parietal regions related to reward processing (Table IV-4). The largest cluster included bilateral superior and middle frontal gyri, extending into bilateral pre/postcentral gyri, supplementary motor area, anterior and middle cingulate cortex, insula, caudate, and thalamus. Additionally, there were clusters in left middle frontal
gyrus extending into the orbital frontal gyrus, bilateral middle cingulate cortex, and left angular gyrus extending to the middle occipital gyrus. Lastly, there was a large cluster including bilateral precuneus extending into bilateral cuneus, calcarine sulcus, superior and middle occipital gyri, and cerebellum. The main effect of Group indicated that adolescents with SMOB showed reduced activation for reward than no reward relative to adolescents with HW in bilateral middle frontal gyrus (Table IV-4; Figure IV-2A). Lastly, the Group x Reward Value interaction indicated that adolescents with SMOB showed reduced activation for high reward than no reward relative to adolescent with HW in the precentral gyrus ($p_{\text{Corrected}} = 0.02$) and posterior cingulate cortex (PCC) extending into precuneus ($p_{\text{Corrected}} = 0.02$), but did not differ in activation from adolescents with HW for the low (precentral: $p_{\text{Corrected}} = 0.98$; PCC: $p_{\text{Corrected}} = 0.89$) or medium (precentral: $p_{\text{Corrected}} = 0.47$; PCC: $p_{\text{Corrected}} = 0.99$) reward contrasts (Table IV-4; Figure IV-2B). Further, while adolescents with SMOB did not show differences in PCC response between high and low reward contrasts ($p_{\text{Corrected}} = 0.20$), adolescents with HW showed greater PCC activation for the high than low reward contrast ($p_{\text{Corrected}} = 0.01$; Figure IV-2B). Thus, during anticipation of monetary reward, adolescents with SMOB showed reduced engagement of bilateral frontal control regions, reduced engagement during high reward in the motor cortex, and reduced sensitivity to increasing reward value in the PCC.

**Reward Related Decision Making**

For behavioral outcomes, one-way ANCOVAs were conducted for number of pumps on trials where the balloon did not pop, balloons popped, and total points. The covariates were not related to number of pumps (maternal education: $p = 0.56$; IQ: $p =
0.52), balloons popped (maternal education: p = 0.63; IQ: p = 0.31), or points earned
(maternal education: p = 0.84; IQ: p = 0.56). None of the outcome measures differed by
Group (pumps: F(1, 52) = 0.15, p = 0.70, ηp² < 0.01; popped: F(1, 52) = 0.11, p = 0.74,
ηp² < 0.01; points: F(1, 52) = 0.27, p = 0.61, ηp² = 0.01), indicating that obesity status did
not impact behavioral performance on the BART.

For the Bayesian decision making model (see model 3; Wallsten et al., 2005),
gamma generalized linear regressions were conducted for two parameters: 1) Reward
sensitivity (γ parameter), which indexes sensitivity to gain; and 2) Response Consistency
(β parameter), which indexes the extent to which participants’ behavior is consistent with
their own evaluation of risk, such that individuals with higher values are more likely to
adapt behavior to changing reward contingencies. As done in previous studies (Bishara et
al., 2009; Rolison et al., 2012), Bayesian Information Criteria was used to test model fit
with 92% of participants (non-obese: 26, obese: 29) showing a better fit for the Bayesian
learning model than a model assuming no learning (binomial test: t(59) = 10.75, p <
0.01). The 5 participants who did not show a better fit for the Bayesian model were
removed from analyses. The covariates were not related to reward sensitivity (maternal
education: p = 0.66; IQ: p = 0.45) or response consistency (maternal education: p = 0.34;
IQ: p = 0.29). Reward sensitivity did not show an effect of Group (β(se) = -0.16 (0.16), t
= -0.96, p = 0.31). However, response consistency showed an effect of Group (β(se) = -
0.48 (0.24), t = -1.98, p = 0.05) such that predicted response consistency for adolescents
with SMOB was almost a third lower than adolescents with HW (eβ = 0.62). This
indicates that despite no differences in behavioral outcomes, adolescents with SMOB had
behavior that was less consistent with their own reward/risk evaluations.
Table IV-4. Group x Reward Value Analysis of Variance: Peak Activations from Significant Clusters for the Monetary Incentive Delay Task, Controlling for Mean Motion Scan-to-Scan and Age.

<table>
<thead>
<tr>
<th>Region (BA)</th>
<th>H</th>
<th>Volume</th>
<th>F</th>
<th>x</th>
<th>y</th>
<th>z</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Main Effect of Group: Not Obese &gt; Obese</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle Frontal Gyrus and Inferior Triangularis (46, 10)</td>
<td>L</td>
<td>189</td>
<td>-3.44</td>
<td>-40</td>
<td>52</td>
<td>4</td>
</tr>
<tr>
<td>Middle Frontal Gyrus and Inferior Triangularis (46, 9)</td>
<td>R</td>
<td>241</td>
<td>-3.82</td>
<td>46</td>
<td>24</td>
<td>46</td>
</tr>
<tr>
<td><strong>Main Effect of Load</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle and Orbital Frontal (10, 11)</td>
<td>L</td>
<td>857</td>
<td>17.61</td>
<td>-34</td>
<td>58</td>
<td>-12</td>
</tr>
<tr>
<td>Middle Cingulate Cortex (23)</td>
<td>R/L</td>
<td>365</td>
<td>11.68</td>
<td>-4</td>
<td>-20</td>
<td>30</td>
</tr>
<tr>
<td>Superior and Middle Frontal Gyri, Anterior and Middle Cingulate Cortex, Insula, Caudate, Thalamus, Precentral/Postcentral Gyri, Supplementary Motor Area, and Inferior Parietal Lobule</td>
<td>R/L</td>
<td>19,643</td>
<td>37.29</td>
<td>-8</td>
<td>10</td>
<td>-4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>25.45</td>
<td>30</td>
<td>18</td>
<td>-8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>21.47</td>
<td>-48</td>
<td>-10</td>
<td>54</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>19.93</td>
<td>-36</td>
<td>-22</td>
<td>58</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>15.89</td>
<td>2</td>
<td>6</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>13.93</td>
<td>42</td>
<td>54</td>
<td>2</td>
</tr>
<tr>
<td>Middle Occipital and Angular Gyri (40)</td>
<td>L</td>
<td>450</td>
<td>14.87</td>
<td>-30</td>
<td>-50</td>
<td>30</td>
</tr>
<tr>
<td>Cuneus, Calcarine Gyrus, Superior/Middle/Inferior Occipital Gyri, and Cerebelum</td>
<td>R/L</td>
<td>13,986</td>
<td>34.84</td>
<td>20</td>
<td>-94</td>
<td>-4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>29.3</td>
<td>-12</td>
<td>-100</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>23.2</td>
<td>12</td>
<td>-94</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>14.9</td>
<td>-2</td>
<td>-78</td>
<td>0</td>
</tr>
<tr>
<td><strong>Group X Reward Value Interaction</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Precentral Gyrus (6)</td>
<td>L</td>
<td>126</td>
<td>12.37</td>
<td>-34</td>
<td>8</td>
<td>42</td>
</tr>
<tr>
<td>Middle Cingulate Cortex and Precuneus (32, 31)</td>
<td>L</td>
<td>214</td>
<td>11.38</td>
<td>-10</td>
<td>-28</td>
<td>34</td>
</tr>
</tbody>
</table>

a: volume measured in mm^3; b: peak F value derived from the Group x Reward Value analysis of variance
BA: Broadmann's Area; H: hemisphere

Episodic Memory

Table IV-5. Peak Activations from Clusters Showing Greater Activation for Adolescents Without than With Obesity During Encoding for Episodic Memory, Controlling for Mean Motion Scan-to-Scan and Age.

<table>
<thead>
<tr>
<th>Region (BA)</th>
<th>H</th>
<th>Volume</th>
<th>t</th>
<th>x</th>
<th>y</th>
<th>z</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-Obese &gt; Obese</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior Orbital Gyrus and Rectus (25, 47)</td>
<td>R</td>
<td>278</td>
<td>-4.78</td>
<td>12</td>
<td>20</td>
<td>-18</td>
</tr>
<tr>
<td>Parahippocampal Gyrus and Hippocampus (28, 35)</td>
<td>R</td>
<td>210</td>
<td>-4.44</td>
<td>28</td>
<td>-34</td>
<td>-10</td>
</tr>
<tr>
<td>Inferior Parietal Lobule (40)</td>
<td>R</td>
<td>171</td>
<td>-4.06</td>
<td>46</td>
<td>-40</td>
<td>52</td>
</tr>
<tr>
<td>Superior Parietal Gyrus and Precuneus (7)</td>
<td>L/R</td>
<td>613</td>
<td>-4.85</td>
<td>-14</td>
<td>-62</td>
<td>44</td>
</tr>
</tbody>
</table>

a: volume measured in mm^3; b: peak t-value derived from the general linear model
BA: Broadmann's Area; H: hemisphere
For behavioral analyses, a one-way ANCOVA was conducted for corrected recognition accuracy (percent correct – percent false alarms) for scenes viewed during encoding. The covariates were not related to recognition accuracy (maternal education: p=0.53; IQ (p=0.16). Corrected recognition accuracy did not differ by Group (F(1, 43) = 0.09, p = 0.77, η² < 0.01; Table IV-2), indicating obesity status did not impact recognition memory.

Figure IV-3. Clusters Showing Greater Activation for Adolescents Without than With Obesity During Encoding for Episodic Memory, Controlling for Mean Motion Scan-to-Scan and Age; p<0.05, corrected.

For imaging analyses, adolescents with SMOB showed reduced activation for subsequently remembered than forgotten scenes relative to adolescents with HW in frontal, medial temporal lobe, and parietal regions (Table IV-5; Figure IV-3). Clusters included the right orbital frontal gyrus extending into the rectus, the right hippocampal and parahippocampal gyri, and right inferior parietal lobule. The largest cluster consisted of bilateral superior parietal gyrus extending into the right precuneus. Thus, despite no behavioral differences in recognition memory, adolescents with obesity showed
decreased neural engagement during encoding of visual information in regions subserving memory processing.

**Discussion**

This was the first fMRI study in adolescents with obesity that did not use food stimuli during executive and reward tasks and the first to examine episodic encoding. Behaviorally, adolescents with severe obesity, relative to those without, showed worse working memory during more difficult loads, slower response speed during the MID, and reward-related decision making behavior that was less consistent with their own risk/reward evaluation. Imaging revealed that adolescents with severe obesity, relative to those without, had greater activation during working memory, but reduced activation during reward anticipation and episodic memory. The mixed pattern of activation results may be related to the amount of cognitive effort required as sub-ceiling working memory performance indicates that the N-Back cognitive taxing while the MID task modeled reward anticipation during passive cue viewing and episodic encoding used an incidental sorting task rather than an intentional memory encoding task. These results, for the first time, showed alterations in functional neural circuitry subserving executive, reward, and mnemonic function.

Although working memory deficits have been observed behaviorally in pediatric obesity (Reinert et al., 2013), no other study has examined the functional neural underpinnings of these deficits in adolescents with obesity. In addition to showing overall slower reaction times, adolescents with severe obesity showed lower accuracy relative to those without obesity during the high load (3-back), but not lower loads (1- and 2-Back). Despite no behavioral differences between groups for 1- and 2-back loads, adolescents
with severe obesity had greater activation during working memory than adolescents without obesity in regions that are canonically associated with working memory (e.g., anterior insular, striatal, and temporal; Rottschy et al., 2012), suggesting greater effort was required to achieve the same level of performance as adolescents without obesity. Differences in striatal activation, in particular, may be related to differences in the ability to flexibly update what is being held in working memory. Updating has been thought to occur via a gating mechanism (Badre, 2012; Chatham & Badre, 2015) subserved by basal ganglia-frontal cortex signaling (Cohen, Braver, & Brown, 2002; Frank, Loughry, & O’Reilly, 2001). Indeed, a recent review showed that abstracts including the word “updating” were more likely to report significant basal ganglia clusters than those that did not include “updating” (Chatham & Badre, 2015). Thus, it is possible that observed working memory deficits are at least partially due to disrupted updating and altered frontal-striatal functional neural circuitry.

Adolescents with severe obesity also showed altered functional neural circuitry related to reward anticipation, which may be related to differences seen during reward-related decision making. During anticipation of monetary reward, adolescents with severe obesity showed reduced activation relative to adolescents without obesity in bilateral middle frontal gyrus. This parallels reduced prefrontal activation to food stimuli in adults and children with obesity (Brooks et al., 2013), suggesting decreased engagement of frontal control regions regardless of reward type. Alternatively, it is possible that adolescents without obesity more actively engaged the mapping between the cue value and expected reward outcome as lateral prefrontal activation has been associated with rule-outcome associations (Dixon & Christoff, 2012). Additionally, there was a
significant interaction between reward value and obesity status in the PCC such that adolescents with severe obesity did not show differences in activation across reward value, while adolescents without obesity showed greater activation for high than low rewards. PCC signaling has been associated with subjective valuation of reward (Bartra, McGuire, & Kable, 2013) and discrepancy between predicted and actual reward (McCoy, Crowley, Haghighian, Dean, & Platt, 2003). Thus, although altered functional neural circuitry may be related to decreased sensitivity to reward value, given the groups did not differ in reward sensitivity during the BART it is more likely related to reduced ability to accurately map anticipated or expected reward value.

Although there was evidence of hypo-responsivity to reward in adolescents with severe obesity, no differences in activation were evident in the ventral striatum, a key region in reward-related networks (Silverman, Jedd, & Luciana, 2015). The literature has not yet parsed whether obesity is associated with hypo- or hyper-responsivity of the ventral striatum, but a dynamic model has been proposed to integrate mixed findings in the literature. It posits that individuals with overweight are more likely to show hyper-responsivity while individuals with obesity are more likely to have a blunted dopaminergic response resulting in reduced striatal activity (Burger & Stice, 2012). Indeed, BMI has been shown to have a curvilinear relationship with activation in the ventral striatum during anticipation of monetary rewards such that adults with overweight had comparably greater activation than those with healthy weight or obesity (Verdejo-Román, Vilar-López, Navas, Soriano-Mas, & Verdejo-García, 2017). This finding parallels results from a positron-emission tomography study showing the highest striatal dopamine binding potential in adults with overweight and comparably lower binding
levels in adults with healthy weight or obesity (Horstmann, Fenske, & Hankir, 2015). Although we were unable to test for it due to the bimodal distribution of BMI, it is possible that the lack of differences in striatal responsiveness between adolescents with and without severe obesity may be due to a curvilinear relationship between activation during anticipation of reward and BMI.

In addition to altered functional neural circuitry underlying reward anticipation, adolescents with obesity showed biases during reward related decision making. This study found no differences in performance during the BART (i.e., total points, balloons popped). However, the failure to find behavioral differences between children with and without obesity on reward-related risk taking tasks is not uncommon in the literature (Groppe & Elsner, 2014; Guerrieri et al., 2007; Scholten et al., 2014) despite evidence for increased reward sensitivity in pediatric obesity (Kulendran et al., 2014). Thus, using decision making models is important to identify possible decision making biases that are not apparent in performance measures of risk-taking tasks. Using the BART decision making model (Wallsten et al., 2005) this study showed that adolescents with severe obesity were less likely to adapt behavior to their own risk/reward evaluation than adolescents without obesity. Given that neural recordings have shown the PCC also carries information about risk and reward uncertainty (McCoy & Platt, 2005), it is possible that these findings are related to the differences seen in PCC related neural circuitry during reward anticipation.

This is the first study to examine the effect of obesity on the neural underpinnings of memory, with almost no previous behavioral research examining the effect of pediatric obesity on memory. The current study showed no group differences in recognition
performance, which is line with the previous finding showing no association between adipose tissue volume and item memory in children (Khan et al., 2015). However, the same study showed a negative association between adipose tissue volume and associative memory in children (Khan et al., 2015), indicating that more complex forms of mnemonic function may show deficits associated with pediatric obesity. Despite no behavioral differences in recognition memory, adolescents with severe obesity showed reduced engagement during encoding of subsequently remembered than forgotten images relative to adolescents without obesity in frontal, hippocampal, and parietal regions. The hippocampus, a key region involved in episodic encoding, has been shown to be sensitive to alterations in metabolic health and insulin signaling, with high-fat diets leading to worse memory in animals (Greenwood & Winocur, 2005; Kanoski & Davidson, 2011; Pistell et al., 2010). Thus, it is possible that reduced engagement of memory networks during encoding may lead to deficits in episodic memory after longer delay periods or when asked to recall more complex details such as associations between items. Future studies are needed to determine how altered functional neural circuitry during encoding relates to and effects episodic memory in pediatric obesity.

These results must be interpreted in light of important limitations that are not specific to this study. First, there was evidence for group differences in SES, index by maternal income and education, and intellectual functioning, indexed by the full-scale IQ. These disparities may have significant impacts on studies examining neurocognitive functioning because lower SES and IQ are not only associated with obesity status (Freidl et al., 2013; Shrewsbury & Wardle, 2008), but also executive functioning (Ardila et al., 2000; Hackman et al., 2010). Although SES and IQ were statistically controlled for, the
true experimental control of matched samples is recommended for future studies. Second, all analyses were correlational in nature, thus, whether these results are related to causal factors or consequences of obesity is unknown. Third, it is possible that some adolescents with severe obesity had undiagnosed or subclinical comorbidities. Obesity results in low-grade, systemic inflammation, which can lead to neuro-inflammation that has the potential of negatively impacting neural (A. A. Miller & Spencer, 2014) and cognitive functioning (Pistell et al., 2010). In order to disentangle causes and consequences of pediatric obesity related to neurocognitive functioning, future studies should incorporate physiological measures (e.g., insulin, inflammation) in longitudinal or intervention (e.g., weight loss) designs.

This was the first study to show altered functional neural circuitry subserving executive, reward, and mnemonic processes in adolescents with severe obesity outside the food context. Since our fMRI protocol did not use food-stimuli, the extent to which these results would hold for food-related processing is not known. Understanding how neurocognitive deficits associated with pediatric obesity affect both food and non-food related behaviors is important to identifying targets for effective prevention and treatment. Although these neurocognitive processes are critical to the regulation of obesogenic behaviors (Dohle et al., 2017; Higgs, 2016), these results suggest that altered neurocognitive function in children and adolescents with obesity has the potential to impact many areas of life including scholastic and adaptive functioning.
V. GENERAL DISCUSSION

This dissertation examined neurocognitive deficits associated with pediatric obesity in order to further clarify the roles of reward, executive, and mnemonic function in pediatric obesity. Known risk factors (e.g., SES, IQ) and comorbidities (e.g., psychopathology) of pediatric obesity were also examined to determine their influence on neurocognitive deficits. Understanding what modulates the association between obesity and neurocognitive function is critically important to the identification of potential causal pathways and the development of prevention and treatment programs.

Consistent evidence for an association between pediatric obesity and neurocognitive deficits across all three experimental approaches emphasizes the robustness of these results and the importance of neurocognitive function in the model of pediatric obesity. Across all studies of this dissertation, pediatric obesity was associated with deficits in executive and reward function with Chapter IV providing direct replication of the working memory and reward related decision making deficits found in Chapter III. Chapter IV also provided the first evidence for altered functional neural circuitry underlying executive and reward processing in adolescents with obesity. Despite convergence of findings, there were also important differences across studies. For example, despite evidence from Chapter II showing that pediatric obesity was associated with an inhibitory deficit, Chapter III did not find an association between pediatric obesity and response inhibition. Below I will discuss how results from different experimental approaches across the three studies inform each other to create a more nuanced understanding of reward function, working memory, and inhibition in pediatric obesity.
Implications: Neurocognitive Functioning

Reward Functioning

Reward related decision making is commonly broken down into three component processes including “liking” (i.e., hedonic motivation), learning reward contingencies, and “wanting” (i.e., desire, driven by saliency and goals; Berridge & Robinson, 2003). Thus, while the ventral striatum is most commonly associated with reward sensitivity, reward function is subserved by a large network of regions including bilateral dorsal striatum, insula, posterior cingulate cortex (PCC), and the frontal operculum (Silverman et al., 2015). While striatal activation did not differ by obesity status, Chapter IV showed that adolescents without obesity had activation in the PCC that scaled with reward value while adolescents with severe obesity did not. The PCC, in particular, has been implicated in the subjective valuation of rewards (Bartra et al., 2013) with neural recordings in monkeys suggesting that PCC signals also carry information about discrepancy between predicted and actual reward and level reward uncertainty and risk (McCoy et al., 2003; McCoy & Platt, 2005).

Probabilistic reward related risk taking tasks like the BART allow for the use of decision making modeling to examine reward related processes biases in addition to observable reward related behavior. Chapters III and IV showed no differences in behavioral outcomes for the BART (e.g., points earned, number of balloons popped), which is in line with findings from Chapter II indicating that reward related risk taking tasks had relatively weaker negative effects of obesity than delay of gratification and delay discounting tasks. One explanation may be that delay discounting and delay of gratification tasks impose a forced choice between known reward outcomes while risk-
taking tasks often have uncertain reward outcomes and require repeated experience over
trials to learn reward contingencies. Additionally, delay discounting has been shown to be
negatively associated with BART behavioral outcomes (e.g., points saved; Mishra &
Lalumière, 2016), possibly because “saving” points becomes an immediate reward.
Therefore, differences in reward sensitivity in pediatric obesity may be masked by greater
delay discounting. Using the BART decision making model (Wallsten et al., 2005),
Chapters III and IV showed that children and adolescents with obesity were less likely to
adapt behavior according to their own risk/reward evaluation. Given the role of the PCC
in the evaluation of risk and reward uncertainty (McCoy & Platt, 2005), it is possible that
the association between pediatric obesity and less adaptive behavior during the BART is
related to differences in PCC neural circuitry seen during reward anticipation. Together,
these findings suggest that reward-related decision making deficits in pediatric obesity
may extend beyond differences in reward sensitivity (i.e., “liking”) to the reward learning
and PCC related reward processing.

**Working Memory**

Working memory, which is the maintenance and manipulation of information in
the mind (Diamond, 2013), has a limited capacity (Oberauer, Farrell, Jarrold, &
Lewandowsky, 2016). Thus, as the number of items required to be maintained increases,
performance is expected to decline due to limited cognitive resources and increased
interference between representations of the items held in mind (Oberauer et al., 2016).
Chapters III and IV showed that pediatric obesity was associated with greater declines in
performance as working memory load increased, such that working memory deficits were
only apparent under higher loads. The effect of load may help explain why Chapter II
showed relatively weaker negative effects of obesity for working memory than other executive processes because differing working memory loads across studies could lead to greater variability and a weaker average effect. It is also possible that the use of span tasks in the literature resulted in weaker effects of obesity as these tasks require the maintenance and manipulation of information, but lack dynamic updating required in the N-Back tasks used in Chapters III and IV.

Although not always included in conceptual models, updating is an important and adaptive component of working memory as it allows for the incorporation of new information and contexts. Working memory maintenance and manipulation are subserved by largely overlapping frontal-parietal networks (Veltman, Rombouts, & Dolan, 2003), with prefrontal regions thought to exert top-down control on posterior regions that store working memory item representations (Lara & Wallis, 2015). Updating, on the other hand, has been hypothesized to function via a gating mechanism (Badre, 2012; Chatham & Badre, 2015) subserved by the basal ganglia (Cohen et al., 2002; Frank et al., 2001) and potentially driven by phasic dopaminergic signaling (Cohen et al., 2002; D'Ardenne et al., 2012). Across studies of working memory, abstracts using the word “updating” were significantly more likely to report activation clusters in the basal ganglia than those that did not use the word “updating” (Chatham & Badre, 2015). Similarly, Chapter IV showed greater activation in adolescents with than without severe obesity in the caudate and putamen. Thus, it is possible that working memory deficits in pediatric obesity are at least partially due updating and inefficient gating in the basal ganglia.
Inhibition

Although inhibition, which is the ability to withhold a prepotent response, was initially identified as one of the three latent factors of executive functioning (Miyake et al., 2000), recent work has suggested that inhibition does not represent a unique executive process (Friedman & Miyake, 2017). Rather than a distinct inhibitory factor, Friedman and Miyake (2017) proposed a common executive factor that loads onto and influences working memory and cognitive flexibility/shifting. Indeed, a recent quantitative review showed that despite substantial shared frontal-parietal activation across executive tasks in children, updating and shifting tasks also showed individual unique patterns of activation while inhibitory tasks did not (McKenna, Rushe, & Woodcock, 2017). The association of response inhibition with working memory and shifting is important to consider when examining the pattern of inhibitory deficits associated with pediatric obesity.

Differing levels of working memory and cognitive flexibility required during response inhibition tasks may help explain the contradicting findings related to inhibition. Although Chapter II showed deficits associated with pediatric obesity for response inhibition and interference, Chapter III did not find any differences in response inhibition by obesity status. One possible explanation for the difference in results is that the stop-signal task used in Chapter III used visual stop cues while most of the literature reviewed in Chapter II used auditory stop cues. Since auditory stop cues are cross modal to the visual go cues, it is possible that more working memory and cognitive flexibility were required for the tasks reviewed in Chapter II than the unimodal version used in Chapter III. Alternatively, it is possible that the proportion of stop-signal trials used in Chapter III differed from the studies in Chapter II. As the proportion of stop-cues decreases, the
prepotency of responding to the go stimuli increases and response inhibition becomes more difficult. Increased prepotency of responding may necessitate greater cognitive flexibility as it will be more difficult to switch task sets and engage in the task rule for stop-cues (Verbruggen & Logan, 2008). Additionally, with more infrequent stop trials, it may be more difficult to actively maintain the task rule for stop trials in working memory (Verbruggen & Logan, 2008). Thus, the discordant results seen in Chapters II and III indicate that inhibitory deficits in pediatric obesity may only be apparent under more challenging task configurations that require greater engagement of working memory and cognitive flexibility.

**Model of Pediatric Obesity**

This dissertation examined neurocognitive function in children and adolescents with obesity in order to further elucidate the feed-forward component of proposed model of obesity (Figure I-3). Although the studies included in this dissertation did not test food-related or obesogenic behaviors, they provided consistent evidence for the association between neurocognitive deficits and pediatric obesity. Additionally, this dissertation showed that demographic and health characteristics moderate some, but not all deficits associated with pediatric obesity. Establishing the role of neurocognitive deficits outside the food context builds a foundation upon which the association between neurocognitive function and obesogenic behaviors can be interpreted. Clarifying the role and specificity of neurocognitive deficits in pediatric obesity is an important step in identifying targets for prevention and intervention.

Conceptualizing the neurocognitive deficits associated with obesogenic behaviors as indices of impulsivity may be useful when considering the feed-forward component in
the model of pediatric obesity. Tasks measuring response inhibition, risk taking, and delay discounting are often referred to as measures of impulsivity, possibly conflating these processes (Nigg, 2017). Indeed, despite the presence of negative effects of obesity for inhibition and reward-related decision making, Chapter II did not show an association between impulsivity and pediatric obesity. These findings show that trait impulsivity may be distinct from inhibitory and reward-related process in so far as it was dissociated from inhibitory and reward-related deficits in pediatric obesity. A confirmatory factor analysis identified three latent factors of impulsivity derived from task performance and self-report measures (MacKillop et al., 2016): 1) impulsive choice, characterized by performance on delay discounting assessments; 2) impulsive action, characterized by performance on response inhibition tasks; and 3) impulsive personality traits, characterized by responses on self-report questionnaires. Following this classification system, this dissertation showed that pediatric obesity was associated with deficits in impulsive choice (i.e., reward-related decision making) and impulsive action (i.e., response inhibition), but not impulsive personality traits. These are promising findings as impulsive choices and actions may be more amenable to intervention than personality traits.

In order to develop successful intervention and prevention efforts targeting impulsive choices and actions, it is important to understand how demographic, health, and psychological factors modulate the proposed model of pediatric obesity. Chapter II showed that inhibitory deficits were moderated by age and gender, potentially indicating that obesity has differential effects on inhibition through development and puberty. Similarly, Chapter III showed that sleep health and psychopathology fully mediated the
association between obesity and everyday executive abilities, but not working memory performance in the lab. This is an important distinction when considering a model of pediatric obesity because significant differences in performance on laboratory tasks do not always translate to significant differences in more ecological assessments of daily behavior. Thus, it may be that poor sleep health and internalizing psychopathology serve to exacerbate executive deficits such that they become apparent in everyday executive behaviors. Together, inhibitory and everyday executive deficits fall under the categorization of impulsive actions, which suggests that demographic and health related characteristics impact the association between pediatric obesity and impulsive actions more than impulsive choices.

**Limitations**

Converging evidence across different samples and experimental approaches in this dissertation emphasizes the importance of neurocognitive deficits in obesity. However, these results must be interpreted in light of three limitations common across all studies: 1) lack of causality; 2) confounding variables that were divergent across groups (e.g., SES), and 3) potentially confounding variables that were not experimentally assessed (e.g., medical comorbidities).

All studies included in this dissertation were correlational in nature, thus, causal interpretations could not be made. While Chapter III tested whether the association between pediatric obesity and everyday executive deficits was causally mediated by sleep health and psychopathology, the temporal order of the mediation model was theoretically based. Since children and adolescents were not followed longitudinally or included in an intervention that directly manipulated these factors, it is not possible to determine which
developed first—executive deficits, obesity, or sleep disturbances and psychopathology. Future studies should employ longitudinal or intervention methods to determine the causal role of executive deficits in the development of pediatric obesity and/or the causal role of pediatric obesity and associated comorbidities in the development of executive deficits.

As with many studies pertaining to pediatric obesity, the primary confounds observed in this dissertation were related to socio-demographic factors. There was evidence for group differences in SES, index by parental income and education, and intellectual functioning, indexed by the full-scale IQ. In the United States, pediatric obesity is associated with both lower SES and IQ (Freidl et al., 2013; Shrewsbury & Wardle, 2008), which is particularly relevant for studies examining neurocognitive function because SES and IQ covary with executive function independently of obesity status (Ardila et al., 2000; Hackman et al., 2010). Chapter II provided evidence that disparities in SES and IQ did not moderate cognitive deficits associated with pediatric obesity, however, only a limited number of studies included the information required to test this effect. Thus, although there is promising evidence that observed deficits are independent of socio-demographic differences, Chapters III and IV statistically controlled for both SES and IQ.

In addition to differences in measured demographic and cognitive factors, children and adolescents are at greater risk for serious medical comorbidities. Although the first two studies presented here only included children and adolescents without known medical comorbidities related to pediatric obesity, it is possible that some children and adolescents with obesity had undiagnosed or subclinical comorbidities. Individuals with
obesity have increased levels of free-fatty acids, which can lead to inflammation (A. A. Miller & Spencer, 2014) and insulin dysregulation (Zhang et al., 2009). Increased inflammation negatively impacts neural functioning (A. A. Miller & Spencer, 2014; Pepping, Freeman, Gupta, Keller, & Bruce-Keller, 2013) and can potentially lead to cognitive declines (Pistell et al., 2010). Therefore, it is important for future studies to explicitly measure and examine the role of subclinical individual differences in inflammation and metabolic health on neurocognitive functioning.

**Future Directions**

Although there is a growing foundation of research addressing the feed-forward component of proposed model, little is known about the role of obesity related comorbidities in neurocognitive dysfunction. In order to empirically address causality in the feed-back loop of obesity, studies have begun to capitalize on weight-loss interventions. In both children and adults, weight-loss surgery has been associated with improved executive function and memory (Thiara et al., 2017). Similarly, a small pilot study using a sample of the adolescents included in Chapter IV showed that after weight loss surgery patterns of activation during working memory and reward anticipation became more similar to those seen in adolescents without obesity (Pearce et al., 2017). Despite promising data indicating improvements in neurocognitive function after weight-loss, the mechanisms behind the observed improvements is still unknown.

One of the most promising mechanisms to target in future research is inflammation for three reasons: 1) onset of chronic, low grade inflammation occurs before the onset of more serious medical co-morbidities (Margioris, 2009); 2) it is sensitive to changes in weight and health status; and 3) there is initial evidence that it
may lead to neuro-inflammatory processes that can impact neurocognitive function (A. A. Miller & Spencer, 2014; Spyridaki et al., 2016). If changes in systemic inflammation track changes in neurocognitive function after surgical or other weight loss interventions it will provide initial evidence for its role as a feedback mechanism in pediatric obesity. Understanding what changes with weight loss and how those changes impact neurocognitive function is important in identifying mechanisms and treatment targets.

**Conclusion**

The findings from this dissertation emphasize the importance of neurocognitive deficits in the development of pediatric obesity while also recognizing the importance of contextual factors such as SES, age, and medical and psychopathological comorbidities. By examining how individual differences within children and adolescents with obesity relate to neurocognitive functioning, it is possible to identify new potential mechanism or paths through with obesity develops or is maintained. The proposed model provides a framework for future empirical studies to identify and test targets for early prevention and treatment of pediatric obesity.
APPENDIX A: REFERENCES INCLUDED IN META-ANALYSIS MODELS


Matton, A., Goossens, L., Braet, C., & Vervaet, M. (2013). Punishment and reward sensitivity: are naturally occurring clusters in these traits related to eating and


95
Control and Symptoms of ADHD in Preschool Children. PLoS ONE, 7(11), e49131.


APPENDIX B: SUPPLEMENTARY MATERIALS FOR CHAPTER III

Measures and Procedures

**Reward-related Decision-Making.** The Balloon Analog Risk Taking Task (BART; Lejuez et al., 2002) consisted of 30 balloon trials for pumping up balloons. The probability of popping a balloon changed with each pump such that the first pump represented a 1/128 chance of popping, the second a 1/127 chance, and so on until the 128th pump which would result in a 1/1 chance of popping, resulting in an average popping point of 64 pumps. Participants were instructed to pump up balloons without popping them, winning 10 points for each successful pump and losing all following popping. Points saved were exchanged for $5, an amount kept equal across participants for ethical reasons, but undisclosed to participants.

**Response Inhibition.** A visual SST (Verbruggen et al., 2008), consisted of three, 3-minute blocks with 72 trials each. During each trial, a fish (go stimulus) facing either left or right was presented in the center of the screen until the participant responded with a button marked “L” or “R”, respectively. A white net (the stop signal) was presented at a variable delay after the fish stimuli (go signal) during 1/3 of the trials. Participants were instructed not to respond if the white net appeared. The first stop-signal of each block occurred after a 250 ms delay, with the delay increasing or decreasing 50 ms after each successful or unsuccessful stop, respectively, in order to maintain ~0.5 probability of successful inhibition. Between each trial, a white fixation circle was presented on the center of the screen for 500 ms.

**Working Memory.** Participants completed a letter N-back task with consonants only (1000 ms exposure, 2000 ms inter-trial-interval) in two runs, 1-back and 2-back, in
counterbalanced order. Each run comprised 60 trials (15 targets) and lasted 2.5 mins.

Participants were instructed to press a button on the keyboard when the letter presented was the same as the letter presented $N$ trials previously (1-back: ‘R’-‘L’-‘L’; 2-back:‘M’-‘K’-‘M’), with a greater working memory demand for 2-back than 1-back.
REFERENCES


Bishara, A. J., Pleskac, T. J., Fridberg, D. J., Yechiam, E., Lucas, J., Busemeyer, J. R.,


Associations of reward sensitivity with food consumption, activity pattern, and BMI in children. *Appetite, 100*, 189–196.


Horstmann, A. (2017). It wasn't me; it was my brain - Obesity-associated characteristics of brain circuits governing decision-making. *Physiology & Behavior, 176*, 125–133.


Obesity, 38(4), 547–551.


